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FBIS-UST-95-033 **CONTENTS** *21 August 1995*

MATERIALS SCIENCE

ENGINEERING AND EQUIPMENT

LIFE SCIENCES

Structural State of Interfaces in Self-Reinforced Aluminum Nitride

957A0887A Kiev METALLOFIZIKA I NOVEYSHIYE TEKHOLOGII in Russian Apr 95 No 4, (manuscript received 15 Nov 94) pp 45-51

[Article by G. S. Oleynik, A. V. Kotko, N. V. Danilenko, and O. A. Shevchenko, Institute of Materials Technology, Ukrainian Academy of Sciences; UDC 669.018.45:539.21]

[FBIS Abstract] The microstructure of self-reinforced aluminum nitride with the indicated typical structure was studied. Specimens produced from aluminum nitride powder, sintered in the the form of initial porous compactions in a nitrogen medium at 1,900°C, were investigated in an electron microscope. Structural studies of the specimens in the electron microscope compared thin foils and angular replicas to natural fractures. The electron microscope study revealed three types of grains and six types of interfaces in the microstructure of the aluminum nitride. The differences in the structure are determined by the presence of polytypes in the material. All the varieties of the grains and boundaries are noted and the most typical combinations and morphological characteristics are shown. The strong distortion of the extinction contours was caused by compressive stresses. Twinning in the AlN [aluminum nitride] polytypes indicates there is yet another variety of intragrain boundaries in the specimens, i.e., twin boundaries. The study shows how significant the effect of polytype formation in the materials is on the structural state of the grains and interfaces in the polycrystalline material, and indicates that polytype formation is a method of regulating the strength of the materials. Figures 2; references 17: 10 Russian, 7 Western.

Multilayer Sheet Material Based on Titanium and Its Alloys

957A0892A Kiev PROBLEMY SPETSIALNOY ELEKTROMETALLURGII in Russian No 2, Apr-Jun 95 (manuscript received 24 Feb 95) pp 3-9

[Article by B. I. Medovar, V. Ya. Sayenko, L. B. Medovar, V. I. Kumin, S. R. Gurgu, L. P. Pasoshnikov, Institute of Electroslag Welding imeni Ye. O. Patona, Ukrainian Academy of Sciences; UDC 669.187.56.001.2]

[FBIS Abstract] Multilayer sheet material based on titanium and its alloys was produced with different combination of the layers, and its ductile characteristics were evaluated. An industrial technique was developed at the Institute of Electroslag Welding imeni Ye. O. Paton to produce multilayer material based on VT1-0 titanium and VT-23 high-strength alloy. The specimens, produced by the autovacuum pressure welding method and edge-welded in vacuum-tight seams, were rolled on an ordinary rolling mill. Two- and three-layer packs were assembled from VT-23 plates 25 mm thick and from VT1-0 titanium plates 15 and 30 mm thick, measuring 250 by 250 mm. The contact surfaces of the plates were machined and were degreased with acetone prior to assembly. The packs were seamed along the edge by argon arc welding with VT1-0 titanium wire. The packs were then heated in an electric furnace to 1,150 ° C, held for 40 min, and rolled on a laboratory rolling mill into sheets 12 and 25 mm thick. The total reduction of the VT1-0/VT-23 packs comprised 160-710 percent. It was difficult to estimate the effect of total reduction during strength rolling of the packs. Macro- and micro-study of two- and three-layer metal indicated a metal bond and the absence of defects along the line joining the layers. However, the autovacuum pressure welding method does not permit one to regulate the strength of joining the layers in multilayer metal. For this reason, the two- and three-layer material produced by this method does not meet the requirements of quasi-impermeability. When the specimens were subjected to impact tests, they also did not meet the requirements. However, the experiments demonstrated that multilayer mateial consisting of titanium and its alloys may have greater impact strength than titanium alone when produced by the autovacuum pressure welding method. Figures 6; Tables 3; references 10: 9 Russian, 1 Western.

Properties of Thick Plates, Rolled From Large-Capacity Sheet Ingot 4.5 t in Mass of VT1-0 Titanium by Arc-Slag Remelting

957A0892B Kiev PROBLEMY SPETSIALNOY ELEKTROMETALLURGII in Russian No 2, Apr-Jun 95 (manuscript received 24 Feb 95) pp 10-14

[Article by B. I. Medovar, V. Ya. Sayenko, V. I. Kumysh, L. B. Medovar, A. G. Bogachenko, B. B. Fedorovskiy, I. A. Lantsman, V. A. Ryabinin, V. V. Shepelev, L. P. Pasoshnikova, S. S. Kazakov, N. M. Khoroshilov, Institute of Electroslag Welding imeni Ye. O. Patona, Ukrainian Academy of Sciences, Kiev, Alchev Metallurgical Combine, Dneprospetsstal Plant, Zaporozhe, Ukrainian Ministry of Industry, Kiev; UDC 669.187.56.001.2]

[FBIS Abstract] The isotropicity of the mechanical properties of thick titanium plates, produced by rolling large-capacity ingots by the arc-slag remelting method, was evaluated. The titanium arc-slag remelting technique, developed at the Institute of Electroslag Welding imeni Ye. O. Paton, permits production of large-capacity ingots weighing 2.5-5 tons or more on exist-

ing electroslag remelting equipment by refitting it. A nitrogen-strengthened slab ingot of VT1-0 titanium, in rectangular section 650 by 1,150 mm and weighing 4.5 t, was produced by the arc-slag remelting method in a crystallizer equipped with a flux gate, on the EShP-5VG electroslag furnace. Macro- and microstudies of a pattern 152 mm thick, and also specimens cut from sheets 14 mm thick along and transverse to the direction of rolling revealed no internal defects in the metal. The results of static tension tests indicate a high level of mechanical properties and isotropicity of hardened titanium 152 mm thick, produced from an arc-slag remelting ingot. The hardened VT1-0 titanium ingot revealed properties that correspond to State Standard 23755-79 in mechanical properties, and is distinguished by high isotropicity of plastic properties. Figures 4; tables 1; references 5: 4 Russian, 1 Western.

Structure and Properties of Titanium Carbide Vacuum Condensers

957A0892C Kiev PROBLEMY SPETSIALNOY ELEKTROMETALLURGII in Russian No 2, Apr-Jun 95 (manuscript received 23 Sep 94) pp 21-23

[Article by B.A. Movchan, T.A. Molodkina, Yu.E. Rudoy, Institute of Electroslag Welding imeni Ye. O. Patona, Ukrainian Academy of Sciences, Kiev; UDC 669.187.526.001.4]

[FBIS Abstract] Especially hard titanium carbide condensates were produced by electron beam evaporation and condensation in a vacuum at high rates of deposition. Their structure, phase composition, and some properties were also studied. The titanium carbide condensates were obtained by electron beam vaporization of titanium and carbon from separate sources, with subsequent deposition of the vapors onto a substrate heated to 720-750 ° C. The carbon was vaporized through a molten tungsten bath, and the melt on the surface of the carbon ingot contributed to formation of an intensive and uniform vapor flux with primary vaporization of the carbon due to the difference in the elasticity of the carbon and tungsten vapors. The method of vaporizing titanium and carbon permits a joint deposition rate of 75 microns/min. The rate of titanium depositions is 50 microns/min and the rate of carbon deposition is 25 microns/min, which is three-fourfold higher than the rate without using a bath. The carbon concentration in the Ti-C condensed material varied as a function of the feed rate of titanium and carbon. The rate of carbon vaporization was 9-13 g/min, while that of titanium was 51-53 g/min. The studies showed that the vapor phase at the indicated rates of carbon vaporization is supersaturated with titanium, and therefore carbon feed rates should be regulated to achieve the required C/Ti ratio. High rates of condensation permit the indicated method to be used to apply TiC coatings to cutting tools. Figures 1; references 3.

Electrohydropulse Machining of Titanium Alloys Upon Vacuum-Arc Remelting

957A0892D Kiev PROBLEMY SPETSIALNOY ELEKTROMETALLURGII in Russian No 2, Apr-Jun 95 (manuscript received 5 May 94) pp 47-56

[Article by B. I. Butakov, Institute of Pulse Processes and Technologies, Ukrainian Academy of Sciences, Nikolayev; UDC 669.187.58.001.3]

[FBIS Abstract] Ingots with minimum zonal liquation in the macro-volumes and with low chemical inhomogeneity in the micro-volumes were manufactured to achieve high-quality semifinished products and finished articles from titanium alloys, using secondary vacuum arc remelting. The effect of electrohydropulse machining on the physical and chemical properties of metal alloys was studied to expand understanding of the mechanism of external effects on the process of crystallization of the alloys. The process significantly increases the rate and degree of diffusion of atoms of impurity and alloying elements between the structural components of metal melts. This indicates that the heat and mass transfer properties on the crystallization front are improved, the zone of concentration recooling before the crystallization front is improved, and the volumetric crystallization of the melt is improved. The mechanical properties of titanium bars 25 mm in diameter were studied on specimens cut in the axial direction and annealed at 870°C for one hour, transferred to a furnace at 650°C for two hours, and cooled in air. The zone of columnar structure was eliminated and the macrograin was pulverized by a factor of 5 upon machining of an industrial ingot 435 mm in diameter, 1,100 mm high from VTZ-1 alloy. Figures 5; tables 3; references 17.

Methods of Optimizing Calibration Curve for Two-Column Ion Chromatography of Anions in Coolant in Nuclear Electric Power Plant

957A0888A Moscow ZAVODSKAYA LABORATORIYA in Russian Apr 95 No 4, manuscript received 27 Apr 94) pp 1-3

[Article by N.V. Bragina and A.D. Karpyuk, All-Russian Scientific Research Institute of Inorganic Materials imeni A.A. Bochvar, Moscow; UDC 543.544]

[FBIS Abstract] The reliability of determination of anions in the coolant in nuclear electric power plants by ion chromatography is of concern, such a determination being conventionally made with the aid of a calibration curves relating each the concentration of a particular anion to a characteristic of the recorded analytical signal. Readings of the signal amplitude yield a higher anion concentrations than do readings of the area (time integral) of the signal peak, the difference widening appreciably as the anion decreases. This inconsistency can be minimized by a finer multilevel calibration making the correlation coefficient come closer to 1.0 over the entire range of measurements. In order to make the data covering the entire range more reliable, it is necessary to increase the sensitivity of measurements and improve the waveform of the chromatographic signal peaks. Both are achievable by addition of modified organic agents to the eluent, particularly suitable being phenol derivatives such as p-nitrophenol and pentafluorophenol. The effectiveness of these techniques was validated experimentally for 0.5-20.0 μg/l Cl-concentrations in water and for SO_4-concentrations in water. Measurements were made with a Tsvet[Color]-3006 chromatograph having a 50 mm high concentrator column and a 200 mm high separator column, both 4 mm wide. As eluent was used a 25 ml large volume of $2.4x10^{-3}$M + $1.0x10^{-3}$M NaOH + $9.0x10^{-4}$M p-nitrophenol. The organic additive reduced the error of Cl- and SO_4-determinations at their lowest concentration levels from 70% to 15% and from 20% to 4% respectively. Another benefit of adding p-nitrophenol is a shorter duration of chromatographic analysis for determination of long retained anions. Tables 5; references 7.

Interaction of Leading Shock Wave at Conical Body With Low-Density Region of Atmosphere

957A0895A St. Petersburg ZHURNAL TEKHNICHESKOY FIZIKI in Russian May 95 Vol 65 No 5, (manuscript received 4 May 94, final version received 14 Oct 94)pp 31-40

[Article by O.M. Veliko, V.D. Urlin, and B.P. Yakutov, Russian Federal Nuclear Center, Arzamas (Nizhnegorod Oblast); 01;03]

[FBIS Abstract] A mathematical model is constructed describing the evolution of a precursor of a conical shock wave at the surface of a cone flying at supersonic speed, this model being designed for a numerical analysis of the influence of that precursor on the aerodynamics of a smooth conical body. In the physical model a conical shock wave is generated by a cone with a rounded nose tip entering a homogeneous originally quiescent atmosphere at a zero angle of attack and some initial velocity. At time t= 0 a part of the leading shockwave makes contact with a rarefied transverse layer of the atmosphere, a rectangular low-density channel whose axis is perpendicular to the axis of the cone and whose width is much smaller than the length of the cone. The pressure in this channel is equal to the quiescent atmospheric one, but the air density in it is much lower than that of atmospheric air. The problem of simulating the evolution of such a precursor on a conical shock wave is solved as an axisymmetric reverse problem, by letting a supersonic air stream with its low-density channel flow past a stationary cone at that quiescent velocity. Air is assumed to be a nonviscous gas which does not conduct heat. Its motion is described the three-dimensional system of nonsteady-state Euler equations, this system being closed by the equation of state for an ideal gas with a constant $\gamma = c_p/c_v =$ 1.4 ratio. The low-density channel has time-dependent boundary conditions at the outer edge of the leading. Thus formulated, the problem is solved numerically in a cylindrical system of coordinates (axis of cone = Z-axis, base of cone in X0Y plane). Calculations according to this scheme have yielded pressure and density isolines, pressure distributions around the cone surface, and the evolution of aerodynamic forces during interaction of the cone with the low-density channel. Both drag and lift coefficients are shown to increase from zero at the beginning to a maximum at about half-time and then decrease to zero at the end of the interaction period. Figures 6; references 11.

Mathematical Model of Leader Discharge Trajectory and Vulnerability of Grounded or Isolated Objects

957A0895B St.Petersburg ZHURNAL TEKHNICHESKOY FIZIKI in Russian May 95 Vol 65 No 5, manuscript received 13 Jan 94, final version received 16 Aug 94) pp 41-58

[Article by N.I. Petrov and G.N. Petrova, All-Union Institute of Electrical Engineering and High Voltage Scientific Research Center, Istra-2 (Moscow Oblast); 01;04]

[FBIS Abstract] Inasmuch as grounded as well as isolated objects are vulnerable when a leader discharge occurs, it is helpful to know the probability of such objects being hit by an imminent lightning. A method of calculating the probability of a hit and flashover on

such objects is proposed which uses the leader discharge trajectory as indicator of subsequent events. The basic physical model of this trajectory treats its behavior, its intricate branching and bending, as a random process in the presence of an electric field. It also takes into account development of a counterdischarge of opposite polarity from the affected object. This physical model is refined by an analysis and evaluation of the role of specific factors in determining the leader discharge step formation and subsequent propagation: 1. gap geometry, 2. overvoltage across the gap, 3. waveform of incident voltage surge, 4. actual electric field intensity in the discharge channel (typically a coaxial one) and the critical electric field intensity, 5. existence of a space charge in the discharge (which requires replacing Laplace's field equation with Poisson's for better precision), 6. statistical characteristics of the leader discharge trajectory, 7. horizontal scattering of affected spots. The mathematical model of the leader discharge trajectory is based on the theory of fractals. The unique feature of the proposed method is that randomness of the leader discharge process and dependence of the leader discharge propagation on the electric field are treated not separately but as two mutually influencing characteristics. It is accordingly shown how calculations by this method will yield the likelihood of a leader discharge propagating toward a grounded object or toward an isolated one and thus the vulnerability of such objects, considering that the probability of a hit and flashover depends also on the polarity of the leader discharge. This method can be applied to a performance evaluation of dynamic lighting arresters, as is demonstrated numerically on lightning rod under typical conditions. An analysis of the results reveals that a protected object is more likely to be hit by a lightning of positive-polarity than by one of negative polarity and that any lightning strikes not only the tip of an arrester but also its lateral surface. The authors thank G.A. Aleksandrov and M.V. Kostenko for helpful discussions. Figures 8; references 33.

Discharge Space in High-Current MagnetoPlasmaDynamic Motor

957A0895C St. Petersburg ZHURNAL TEKHNICHESKOY FIZIKI in Russian May 95 Vol 65 No 5, (manuscript received 12 May 94, final version received 18 Aug 94) pp 59-66

[Article by N.A. Barabanov, Moscow Institute of Aviation; 01;03;04]

[FBIS Abstract] The performance of high-current magnetoplasmadynamic (MPH) rocket motors of the radial type is analyzed theoretically by a method ensuring a fairly reliable agreement between the results of calculations and the results of experimental simulation of real operating conditions. Plasma flow calculations are made in the approximation of quasi-one-dimensional steady flow, which is already known to adequately well describe the distribution and the kinetics of the plasma parameters in the interaction space. Available experimental data on argon-plasma and lithium-plasma motors indicate, moreover, that both viscosity and thermal conductivity of the plasma as well as the Hall effect and the energy dissipation may be ignored. This reduces and simplifies the four equations of magnetohydrodynamics (MHD) to three, while the equation of state pv= mRT is retained. Magnetic induction is treated in the quasi-two-dimensional MHD approximation. The two equations of kinetics of its distribution are formulated accordingly, in a cylindrical (r,z) system of coordinates, assuming that the anode is cylindrical and the electrical conductivity of the plasma is constant. The system of these two equations, reduced to a dimensionless form, has been solved for 10 kA, 20 kA, 21 kA discharge currents with the same 10 g/s argon flow rate in each case and with Dirichlet's boundary condition for the magnetic induction on the anode side. The results are found not to significantly depend on the particular form of that boundary condition. The author thanks G.A. Lyubimov and V.A. Bityurin for discussing this subject at their seminars. Figures 4; references 13.

Effective Method of Calculating Wave Impedance of Bodies of Revolution in Transonic-Speed Range

957A0894A Novosibirsk PRIKLADNAYA MEKHANIKA I TEKHNICHESKAYA FIZIKA in Russian Vol 36 No 3, May-Jun 95 (manuscript received 5 Jul 94) pp 60-68

[Article by M.A. Nayda and A.S. Fonarev, Central Institute of Aerohydrodynamics, Zhukovskiy (Moscow Oblast); UDC 533.6.011]

[FBIS Abstract] The problem of transonic air flow past a long body of revolution is analyzed by applying to it the nonlinear transonic theory of small perturbations. The dimensionless nonsteady-state equation for the velocity potential ϕ according to that theory is $2A\phi_{xt}= B\phi_{xx} + (r\phi)_r/r$ ($A= N_{Ma}(\infty)^2$, $B= 1- A - (\gamma+ 1)A\phi_x$, $N_{Ma}(\infty)$- Mach number of quiescent flow, $\gamma= c_p/c_v$ - power exponent characterizing adiabatic air flow, $V(\infty)$- velocity of approaching stream, L- length of body, ϕ- perturbed velocity potential referred to $V(\infty)L$, longitudinal coordinate x and radial coordinate r referred to L, t- time referred to $L/V\infty$). As constraints are selected nonreflecting far- field boundary conditions [D. Kwak; AIAA JOURNAL Vol 19 No 11, Nov 81]. With pressure on the body and velocity of air expressed so as to account for the axial symmetry of the problem in the approximation of small perturbations,

this equation is solved for successive fixed instants of time by applying the theorem of momentum integrals and the wave impedance of the body then calculated by integration of the pressure along an incident shock wave (or shock waves). Such calculations were made by the numerical method of variable directions using its implicit axisymmetric scheme and the monotonic Engquist-Osher algorithm on a rectangular 121x.81r space grid. They were made for three models with different r/L ratios, each consisting of three parts: 1. nose approximating an ellipsoid of revolution, 2. fuselage in the form of a circular cylinder, 3. tail shaped like a spindle. The results of these calculations covering the $N_{M\infty}$= 0.9-1.07 range reveal how the wave impedance of such bodies depends on the air velocity within this transonic range. The results have been compared and found to agree closely, much closer than the results of integration over the body surface, with experimental data characterizing an aircraft and its equivalent ellipsoid of revolution in the wind tunnel at the the Central Institute of Aerohydrodynamics. Figures 5; references 13.

Experimental Study of High-Frequency Secondary Perturbations in Boundary Layer at Sweptback Wing

957A0894B Novosibirsk PRIKLADNAYA MEKHANIKA I TEKHNICHESKAYA FIZIKA in Russian Vol 36 No 3, May-Jun 95 (manuscript received 15 Jul 94) pp 74-83

[Article by A.V. Boyko, V.V. Kozlov, V.V. Syzrantsev, and V.A. Shcherbakova, Institute of Theoretical and Applied Mechanics at Russian Academy of Sciences, Siberian Department; UDC 532.526]

[FBIS Abstract] An experimental study was made concerning the evolution of traveling waves at a solitary vortex in the boundary layer at a sweptback wing and the attendant transition to turbulence. Tests were conducted at an air velocity of 7 m/s in a 4 m long and 1 m square segment of a subsonic wind tunnel with slight turbulence, the amplitude of velocity fluctuations at that air velocity not exceeding 0.04% of the quiescent air velocity. As the model had been selected a 5.6 mm long and 80 mm thick ogival nose with a transition to two converging on it identical flat surface elements, its high-lift profile featuring a 30° slope angle and a 500 mm wide chord. This model was mounted in a vertical position rigidly between two horizontal plates so that its active profile segment faced the air stream with its plane surface at a zero angle of attack. Stationary perturbations were produced behind a protuberance which had been glued to the active model segment with its one end made smooth end and the other end extended to the idle model segment so as to prevent separations. Velocity measurements were made with a thermoanemometer along the middle segment of the model and thus in the zone almost nonexistent secondary flow, the readings being recorded with an XY-plotter designed so as to allow lifting some constraints on movements of the transducer in the XZ plane. Traveling waves were generated in the boundary layer by conversion of acoustic vibrations into vortical perturbations of the displacement layer at a local surface asperity, the acoustic vibrations having been generated by two dynamic loudspeakers inside a diffuser transmitting sound in the direction opposite to that of the air flow. Measurement and analysis of the frequency spectrum revealed a formation of at least two perturbation wave packets in one vortex, their central frequencies being close to 400 Hz and 1800 Hz respectively. These packets followed very different downstream evolutions patterns. While the amplitude of perturbations in the low-frequency packet was increasing and their spectrum becoming denser, perturbations in the high-frequency packet were becoming weaker and did not directly participate in the transition to turbulence. The high-frequency traveling waves generated by that packet were, however, found to strongly influence the air flow in the boundary layer, namely to accelerate it and thus not only alter the profile of the average velocity but also amplify the low-frequency perturbations. Figures 8; references 13.

Strength and Toughness of Metals Over Wide Range of Deformation Rates

957A0894C Novosibirsk PRIKLADNAYA MEKHANIKA I TEKHNICHESKAYA FIZIKA in Russian Vol 36 No 3, May-Jun 95 (manuscript received 6 May 4) pp 134-140

[Article by V.A. Ogorodnikov, Ye.S. Tyunkin (deceased), and A.G. Ivanov, All-Russian Scientific Research Institute of Experimental Physics, Arzamas; UDC 53.374;662.215.2]

[FBIS Abstract] In connection with the problem of high-speed compression of metal shells toward their center or axis of symmetry at strain rates covering the 10^3-10^6 s^{-1}, a new method of determining their dynamic yield point and dynamic viscosity in the plastic state is proposed, namely on the basis of special compression tests performed on cylindrical shells. Conventional high-speed deformation by explosion of a charge laid on the outer surface of the shell must be modified for such tests so that the shell will not ultimately shatter but retain a neck. This is accomplished by placement of additional shields about as thick as the shell wall on the outer surface of the charge, quasi-instantaneous detonation

thus being attainable with a much thinner charge and the shell becoming compressible in the inert necking mode. Under these conditions the entire initial kinetic energy of such a shell is spent on plastic deformation of the shell and thus on work of overcoming the shell's resistance forces. A mathematical model is constructed to describe this process, assuming that the shell material is incompressible with a constant yield point. This model was used for interpretation of test data pertaining to cylinders which had been deformed in earlier experiments: 1. grade-3 carbon steel cylinders 16 mm in diameter with a 0.92 mm thick wall and 9 mm in diameter with a 0.93 mm thick wall, loaded by impact causing wall movement with an initial velocity of 640 m/s and 730 m/s respectively; 2. lead cylinders 42 mm in diameter with a 6.3 mm thick wall, loaded by successively stronger impacts causing wall movement with correspondingly higher initial velocities (20.3 m/s - 36.3 m/s - 56.6 m/s). There also had been tested Armco iron cylinders and grade-45 carbon steel cylinders. In this experiment grade-3 carbon steel cylinders 4 mm in diameter with a 1 mm thick wall and 2 mm in diameter with a 0.5 mm thick wall were successfully compressed to a neck at strain rates up to $2x10^6$ s^{-1}, the yield point having been found to rise more steeply within the $3x10^5$-$2x10^6$ s^{-1} range. Figures 5; references 17.

Dynamic Strength of Shells Made of Oriented Fibrous Composite Materials

957A0894D Novosibirsk PRIKLADNAYA MEKHANIKA I TEKHNICHESKAYA FIZIKA in Russian Vol 36 No 3, May-Jun 95 (manuscript received 12 Jan 94, final version received 1 May 94) pp 141-145

[Article by M.A. Syrunin, A.G. Fedorenko, and A.G. Ivanov, All-Russian Scientific Research Institute of Experimental Physics, Arzamas; UDC 624.074.4:678]

[FBIS Abstract] An experimental study of wound cylindrical shells of a composite material was made concerning their dynamic strength under internal pressure due to explosion of a charge inside. The shells were made of about 10 μm thick fibrous glass tape as the reinforcement and epoxy resin as binder. With such a tape were built cylindrical stacks of alternating equally thick and equally 600 mm long two kinds of layers: long sleeves formed by winding the tape at (+/-)45° lay angles into double-helix braids and collars formed by tightly winding the tape at a 90° lay angle into rolls. These skeletons were then impregnated with EDT-10 epoxy compound. Four experimental lots of such shells with a 150 mm inside radius were built produced for mechanical tests. Two lots were produced using general-purpose fibers: one with grade VM-1 fiber (RVMN roving) and one using grade VMP fiber (RVMPN roving); two lots were produced using special-grade fibers developed at the All-Russian Scientific Research Institute of Synthetic Polymer Fibers in Kryukovo (Moscow Oblast): one with grade-R fiber (RRN roving) and one using grade-Kh fiber (RKhN roving). [V- fiber, R- roving, M- material, P- high strength, N- winding]. The wall thickness to radius ratio of with VM-1, VMP, and R fibers was 4.18+/-6%, that of shells with Kh fibers was 2.45+/-2.7%. Each lot was tested for ultimate tensile strength, Young's modulus, ultimate fiber elongation, speed of sound in fiber, and maximum rate of collar expansion. Their properties have been compared with those of analogous shells made with rope of SVM synthetic high-polymer fibers. The results indicate that shells with VM-1 or VMP glass-plastic fibers have a much higher (25% and 45%) load carrying capacity than shells with R or Kh glass-plastic fibers, that of shells with SVM organoplastic fibers approaching that of shells with VMP fibers. All shells made with glass-plastic fibers deform elastically till fracture. Their fracture mechanism is associated with loss of dynamic stability by the radially axisymmetrically vibrating middle part of such a shell under maximum strain during initial expansion, when this strain exceeds the maximum allowable one. The elastic behavior of all the five composite materials was found to be essentially the same within a less than 30% wide range of differences, being determined by the characteristics of the fiber material (Poisson's ratio 0.2) and those of the epoxy resin (Poisson's ratio 0.4, Young's modulus 3000 MPa, density 1230 kg/m^3) as well as by and by the multilayer winding pattern. Figures 1; tables 3; references 17.

Insertion Mutant Francisella tularensis A cole SM Providing Overproduction of Capsular Substance

957A0627A Moscow BIOTEKHNOLOGIYA in Russian Aug 94 No 8, (manuscript received 6 Sep 94) pp 3-6

[Article by A. P. Pomerantsev, O. M. Pomerantseva, V. N. Gerasimov and V. V. Mishchenko, State Scientific Research Institute for Applied Microbiology, Obolensk, Moscow Oblast, 142279; the first paragraph is an abstract; UDC 579.253.2]

[FBIS Translated Text] The determinant of chloramphenicol resistance (Cm^R) of the Sa plasmid, flanked by two direct repeated sequences, was introduced into the gene of the virulent strain *Francisella tularensis A cole*. The clone *F. tularensis A cole SM* obtained as a result of integration of the Cm^R determinant stably inherited the inserted feature, produced chloramphenicol acetyltransferase, had a reduced virulence for laboratory animals and had an increased capacity for synthesizing the capsular substance. The DNA-DNA hybridization method revealed the presence of an amplified form of the Cm^R determinant in the *P. tularensis A cole SM genome*.

The causative agent of tularemia — bacteria of the species *F. tularensis* — are small gram-negative coccobacteria which are subdivided into at least two biological subspecies — *F. tularensis subsp. tularensis* (type A) and *F. tularensis subsp. holarctica* (type B). The type-A bacteria are more virulent for man and in some cases overcome immunity in animals first receiving type-B vaccine strains [2].

Attempts to obtain vaccine strains on the basis of type-A causative agents by means of selection of spontaneous mutants have not led to success and therefore we selected an insertion mutagenesis method successfully employed in obtaining the new vaccine strains *Bacillus anthracis*, *Brucella abortus* and *Yersinia pestis* [3-5].

It was demonstrated earlier that the determinant of chloramphenicol resistance (Cm^R) of the Sa plasmid, flanked by two direct repeated sequences [6], is capable of being inserted into chromosomal DNA of the vaccine strain *F. tularensis 15* (type B) and can be expressed there [7, 8]. Taking these data into account, we made an attempt to insert this same determinant in the gene of the virulent strain *F. tularensis A cole* (type A) for the purpose of selecting clones with weakened virulence and studying their properties.

Experimental Conditions

The strain *F. tularensis A cole*, used as a recipient in cross-over experiments, was provided through the kindness of the Tularemia Laboratory, Microbiology and Epidemiology Institute imeni N. F. Gamaleya (Moscow). The donor strain of the Sa plasmid of *Escherichia coli* (Sa, pSKFT5), as well as the cross-over method, were described in detail in our earlier studies [7-9].

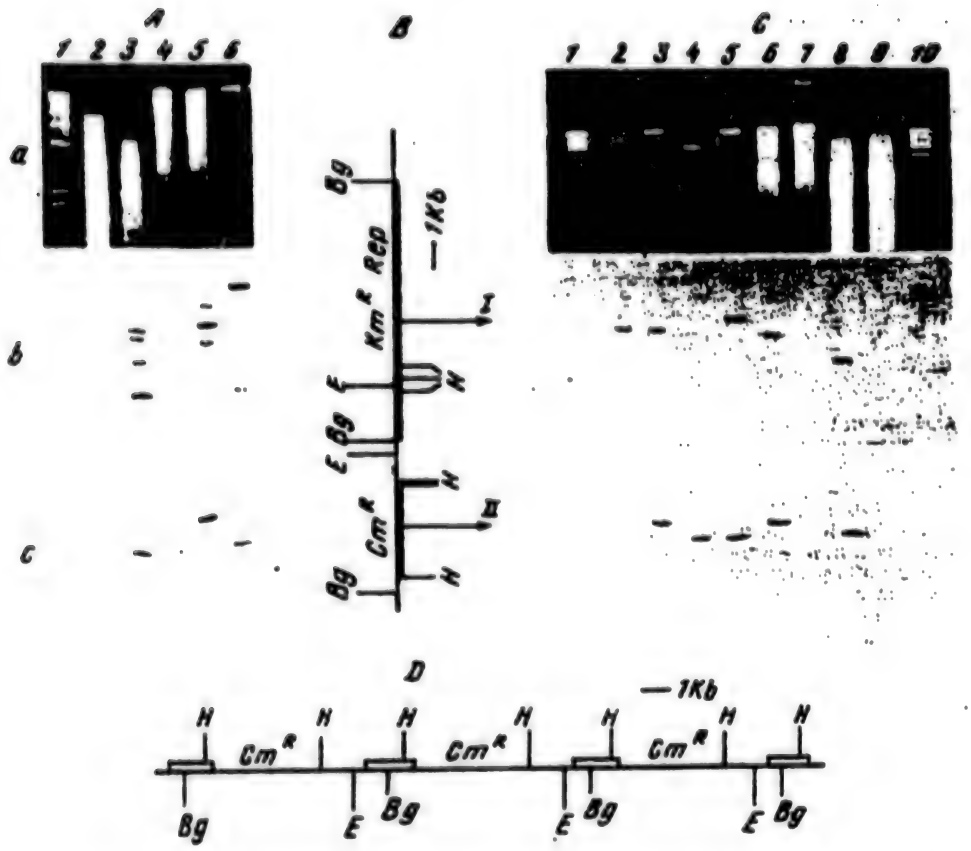

Fig. 1. Sauzerne hybridization of fragments of chromosomal DNA of strains of *A cole* and *A cole SM* with fragments of Sa plasmid, a — electrophoregrams; b — blots after interaction with probe I; c — blots after interaction with probe II; A — soft washing conditions. DNA sequence in slots: 1) lambda phage, HindIII; 2 — *A cole*, HindIII; 3 — *A cole SM*, HindIII; 4 — *A cole*, EcoR1; 5 — *A cole SM*, EcoRI; 6 — Sa plasmid, HindIII. B — fragment of Sa plasmid with indication of probes (defined by solid rectangles). C — hard washing conditions. DNA sequence in slots: 1, 10 — lambda phage, HindIII; 2 — cloned BgIII fragment of Sa plasmid (probe D); 3 — Sa plasmid, BgIII; 4 — cloned in plasmid pBR322 (upper fragment) Cm^R determinant of Sa plasmid (lower fragment, probe II); 5 — Sa plasmid, HindIII; 6 — *A cole SM*, EcoRI; 7 — *A cole*, EcoRI; 8 — *A cole SM*, HindIII; 9 — *A cole*, HindIII; D — amplification of Cm^R determinant of Sa plasmid in chromosome of strain *A cole SM*. Unfilled rectangle — direct repeated sequence, flanking Cm^R determinant of Sa plasmid [6]. Notation: Bg — BgIII; E — EcoRI; H — HindIII.

The isolation of chromosomal and plasmid DNA, their fragmentation by restriction endonucleases, electrophoretic separation of fragments and their visualization were carried out as described in [8, 9].

The hybridization probes used were the HindIII restriction fragment of the Sa plasmid, inheriting the gene of chloramphenicol acetyltransferase (Cat) and the BgIII fragment containing the region responsible for the replication of this plasmid [10]. The indicated fragments were eluted from agarose gels and the methyl biotin-7-desoxyadenine triphosphate method by the nick-translation method in accordance with the Nonradioactive Nucleic Acid Detection System (BRL, United States). DNA- DNA hybridization was accomplished by the Sauzerne method on Hybond nylon filters (Amersham, Great Britain) in accordance with the appended recommendations. After hybridization the filters were washed under soft and hard conditions. In the first case we limited ourselves to incubation of the filters in 1 x SSPE, 0.1 percent SDS at 65° for 15 minutes, in the second case the filters were incubated additionally in 0.1 x SSPE, 0.1 percent SDS at 65° for 10 minutes. The detection of Sauzerne blots was accomplished colorimetrically after their successive processing by a conju-

gate of streptavidin with alkaline phosphatase, nitroblue tetrasol and 5-bromo-4-chloro-3-indolylphosphate. The staining of the blots and their scanning was carried out using a standard set of reagents BluGENE (BRL, United States).

A quantitative determination of polysaccharides in samples of the capsular substance (CS) of the tularemia microbe was carried out using the Molisch test by means of phenol extraction [11]. The CS samples were obtained by the Hood method [12] from cells grown on a dense medium over the course of two days at 37°.

The chloramphenicol acetyltransferase activity (cat) of the investigated lysates was determined spectrophotometrically, as described earlier in [13].

A comparative study of the morphology and fine structure of cells of the tularemia microbe was carried out using a transmissive electron microscope. The morphology and the morphometric characteristics of the microbes were investigated using total preparations of negatively stained cells [14]. The characteristics of the fine structure of the cells was determined by the ultrafine sections method [15]. The detection of the capsular cover of the tularemia microbes was accomplished using the modified method for preparation of bacteria for electron microscope studies [16]. In order to preserve the internal structure of the cells and capsule the microbes were first fixed for a period of two hours in a 2 percent solution of glutaric aldehyde (pH 7.2), incorporated in a 10 percent aqueous melt (45°) of gelatin and additionally fixed with a 2 percent solution of osmium tetroxide in an acetate-barbital buffer (pH 7.0) for 18 hours. The fixed microbes were dehydrated by ethanol and encased in araldite. The sections were obtained using an Ultracut ultramicrotome (Reihert, Austria), additionally contrasted with uranyl acetate and lead citrate [17] and studied using a Hitachi-500 electron microscope at 75 kV.

The virulent properties of the studied strains were evaluated using the LD_{50} values [18] for mice and rabbits infected subcutaneously by 10-fold increasing doses of microbe cells resuspended in a physiological solution.

Results and Discussion

The frequency of transfer of the Sa plasmid from coliform bacteria cells to the cells of the virulent strain *F. tularensis A cole* was 2 x 10^{-8}, which was five times lower than the similar index for cells of the vaccine strain *F. tularensis 15*, previously selected as the recipient [7]. An analysis of Cm^R clones of the strain *A cole*, obtained as a result of conjugation, indicated that as in the case with the vaccine strain some clones inherited the Sa plasmids in an extrachromosomal state and lost it during passivation without selective pressure, whereas others revealed the absence of a plasmid in the lysates, but stably inherited the characteristics of chloramphenicol-resistance during passivation without selective pressure [8]. One of the clones stably inheriting the Cm^R characteristics, attracted attention due to its increased mucosity in comparison with the other clones and the initial strain. This clone, which because of its properties we called *A cole SM* (supermucous), was selected for further study.

In order to confirm the presence of the Cm^R determinant of the Sa plasmid in the chromosome the strain *A cole SM* experiments were carried out for the hybridization of this determinant with chromosomal DNA of the strains *A cole* and *A cole SM*. It is known that the cat gene, ensuring resistance to chloramphenicol, falls within the limits of the HindIII fragment measuring 3.1 kb [10]. Accordingly, precisely this fragment was inserted in the high-copy vector pBR322, which made it possible to isolate it in large quantities and use it as a probe in hybridization.

The absence of resistance to aminoglycosides in the strain *A cole SM* made it possible to express the hypothesis that only the Cm^R determinant of the Sa plasmid was inserted into the chromosome of the strain *A cole*. Earlier such a result was obtained in [19] in a study of the behavior of the Sa plasmid in *Zymomonas mobilis* cells. A probe constituting the middle BgIII restriction fragment of the Sa plasmid was used for proof of this hypothesis in hybridization experiments [10]. This fragment, inheriting the operon of aminoglycoside resistance (Km^R) and the sector of initiation of replication (Rep) of the Sa plasmid, is positioned distally relative to the cat gene and has a total sequence with the region of the right direct repeated sequence flanking the cat gene [9]. The possibility of inheritance of this fragment in coliform bacteria cells in the form of an independent replicon [20] made it possible to clone it in the form of an individual plasmid and quite specifically use it in the hybridization experiments whose results are represented in Fig. 1.

It can be seen that under soft washing conditions, in addition to major fragments, whose intensity is comparable to the intensity of staining of fragments of the Sa plasmid, DNA samples of the strain *A cole SM* exhibit fragments which are not manifested after processing of the blots under hard conditions. A determination of the molecular weight of the major fragments detected during hybridization of probes with EcoRI and HindIII restriction fragments of chromosomal DNA of the strain *A cole SM* revealed that the DNA sector of the Sa plasmid, flanked by direct repeated sequences and inheriting

the cat gene, is found in the chromosome of the strain *A cole SM* in an amplified form; its model is represented in Fig. 1,D. Taking the presented experimental data into account, it is difficult to determine the true number of copies of the cat gene in the amplification, as well as the site specificity of its integration with the chromosome of the strain *A. cole*. However, taking into account data on determination of the dose of the cat gene in the chromosome of the vaccine strain *F. tularensis* [13] and comparing the Cat activity of the lysates of this strain and the strain *A cole SM*, which were identical, it can be postulated that the number of copies of the cat gene in a chromosome of the strain *A cole* also cannot be less than four. The absence of bands in the blots of the HindIII fragments of DNA of the strain *A cole SM* after their hybridization with the BgIII fragment of the Sa plasmid in the region of the large HindIII fragment of the Sa plasmid is evidence that only the Cm^R determinant of this plasmid is integrated into the chromosome of the strain *A. cole*. The result confirmed the hypothesis which we expressed earlier in [8] that in the cells of the tularemia microbe this determinant is a transposon whose integration with the genome of the strain *A cole* was manifested phenotypically, in particular, in the appearance of a strain more mucous than the initial strain.

In a study of the structural-population characteristics of the biomass of the initial and genetically modified strains in the stationary growth phase it was discovered that the microbes form a population with an identically complex structure typical for bacteria of the genus *Francisella*. In these, in addition to cells of round and oval configuration, there are a large number of bacteria of an ellipsoidal and rodlike configuration. The strains also do not differ from one another with respect to cell size (Fig. 2,a,b).

All the bacteria of the initial strain *A cole* were covered by a capsule with distinct contours with a thickness 0.12-0.14 μm. In the preparations a high percentage of the cells (80-85 percent) were distributed individually and in small groups of 2-5 cells, surrounded by a common capsule (see Fig. 2,c). In sections of bacteria of the genetically modified strain *A cole SM*, on the other hand, there was abundant formation of cells of a capsule-like substance, in a thick layer (0.15-0.35 μm) with even edges enveloping large groups of microbes consisting of 5-25 or more cells (see Fig. 2,d). The content of polysaccharides in the CS of *A cole SM* with an identical number of cells in the samples exceeded by a factor 2.5-5 the number obtained for the initial strain.

Another result of the insertion of the Cm^R determinant of the Sa plasmid in the genome of the strain *A cole* was a decrease in the LD_{50} values of the recipient strain with 1 microbe cell (m.c.) for CBA mice and 2 m.c. for rabbits to 216 m.c. or more than 10^{10} m.c. respectively for the strain *A cole SM*. It must be noted here that other phenotypic characteristics of the strain *A cole*, determining its assignment to type-A bacteria (in particular, sensitivity to erythromycin and the capacity to ferment glycerin [2]), were retained in the strain *A cole SM*. The immunization index of the strain *A cole SM* with an immunizing dose 100 m.c. (subcutaneously) for CBA mice with subcutaneous resolution for the strain *A cole* was 2×10^5.

Thus, the strain *F. tularensis A cole SM* was obtained. On the one hand it has protective properties relative to the biotype A of the tularemia microbe and can be used as a prototype of a live tularemia vaccine, and on the other hand, being a superproducer of the CS, can be used when obtaining the polysaccharide component of a chemical vaccine whose development is recently being devoted ever-increasing attention [21]

Fig. 2. Electron microphotographs of bacteria *F. tularensis*: a,b — negatively contrasted cells of the strains *A cole* and *A cole SM* (scale 0.5 μm); c,d — ultrathin sections of cells of strains *A cole* and *A cole SM* (scale 0.4 μm).

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Methodical Approaches to Isolation of Yersinia pestis Vaccine Strains Highly Resistant to Lyophilization

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[Article by N. V. Lopatina and L. A. Natalich, Antiplague Scientific Research Institute, Rostov-na-Donu, 344007; the first paragraph is an abstract; UDC 57.086.132:57.083.1]

[FBIS Translated Text] Vaccine strains of the plague microbe having a high thermal stability and immunogenicity were obtained at the clone level by the multiple lyophilization and selection method. The proposed experimental approaches can be used for stabilizing the cell composition of vaccine strains and the effective vaccines developed on their basis. In the problem of improving a live dry plague vaccine the matter of selecting the vaccine strain has occupied an extremely modest place. For the most part the studies of modern authors have been directed to increasing the immunogenicity of vaccine strains [1-4]. Only a few studies [5-7] have been devoted to the problems involved in the resistance of strains to lyophilization — the principal technological process used in obtaining a vaccine.

The purpose of the study was to obtain vaccine strains of the plague microbe resistant to lyophilization using selection methods at the population and clone levels.

Experimental Conditions

Two strains of the plague microbe were used in the study: Yersinia pestis EV and the strain present in the genome of the determinant of resistance to antibacterial agents [8].

Two series of experiments were carried out. In the first series the resistant strains were selected at the population level using lyophilization as a selection factor. The two strains used in the experiment were subjected to successive triple lyophilization. For this purpose two-day cultures, obtained in CO agar, containing splenic

autolysates with the addition of salts and protein hydrolysate of wheat cuttings [9], were suspended in a protective medium consisting of 10 percent saccharose, 1 percent gelatin and 1 percent thiourea. The suspensions (2 ml in each ampule) were lyophilized using a specially developed scheme [10]. The lyophilized cultures were rehydrated, the number of viable cells was counted and subjected to subsequent lyophilization (singly or doubly).

Table 1. Number of microbe cells in vaccine prepared on basis of singly and doubly lyophilized vaccine strains of plague microbe

Vaccine series	Number of viable cells, billion/ml					
	Y. pestis EV 76			Strain with plasmid resistance		
	Before lyophilization	After lyophilization	%	Before lyophilization	After lyophilization	%
			n = 9			
Initial strain (control)	8.9	4.2	47.2	7.5	3.8	50.6
Singly lyophilized strain	25.7	12.6	49.0	19.0	10.0	52.6
Doubly lyophilized strain	24.8	14.0	56.6	21.9	19.0	54.8

In the second series of experiments the resistant variants were selected at the clone level. For this purpose a study was made of the population composition of the initial, singly and doubly lyophilized strains relative to the degree of resistance of the subcultures to lyophilization. Each colony was suspended in 2 ml of physiological solution and sown on CO agar with subsequent lyophilization in a protective medium with thiourea. The resistance of each subculture was assessed relative to the number of viable cells remaining alive after lyophilization. The subcultures most resistant to lyophilization were cloned, each clone was lyophilized and the most resistant were selected. A resistant clone was cloned once again, etc. On the basis of singly-doubly lyophilized strains and selected clones with increased resistance to lyophilization experimental series of vaccine were prepared which were investigated for viability (percentage of live cells after lyophilization, number of live cells in 1 ml of suspension, billion/ml), immunogenicity (ImD_{50}) [11] and thermal stability (thermal stability index, prediction of vaccine storage times) [12]. The resistance to antibiotics before and after lyophilization was determined for the strain containing the plasmid of resistance to antibacterial agents.

Results and Discussion

The prerequisite for using lyophilization as a selecting factor was the surmised possibility of stabilizing the cell composition of the strain due to the death of cells weakened under the influence of lyophilization stress. Table 1 gives the number of microbe cells in a vaccine prepared on the basis of singly and doubly lyophilized strains.

The data in Table 1 show that the number of cells in a vaccine prepared on the basis of singly and doubly lyophilized strains exceeded the corresponding index in the control series by a factor of 2.5-3. This occurred both due to an increase in the percentage of resistant cells in the population and due to an increase in the rate of multiplication of the lyophilized cultures in the culture medium. The cells subjected to stress evidently acquire a capacity for more intensively reproducing in a nutrient medium under normal cultivation conditions. This capacity is manifested in microorganisms of other taxonomic groups (Saccharomyces cerevisiae, Beauveria bassiana) [13, 14]. Some authors attribute this cell capacity to the biosynthesis of protective proteins stabilizing macromolecules of microorganisms and intensifying their hydrophobic properties. An increase in the number of lyophilization operations to more than three did not result in a substantial increase in the number of resistant cells in the vaccine. Their maximum number was attained after single or double lyophilization of the initial strains.

The cloning of the population makeup of the initial, singly and doubly lyophilized populati ns of the strain Y. pestis EV with subsequent selection of clones resistant to lyophilization indicated that with respect to this criterion the population is exceedingly nonuniform (Table 2).

Table 2. Distribution of clones resistant to lyophilization in initial, singly and doubly lyophilized population of strain Y. pestis EV

Number of strain lyophilizations	Number of studied clones	Percentage of lyophilized clones resistant to lyophilization, %
Initial population	65	7.5
Singly lyophilized population	60	17.5
Doubly lyophilized population	40	12.5

Note: those clones were considered resistant the number of whose cells after lyophilization exceeded by a factor of two or more the similar index for the initial strain.

The data in Table 2 show that the number of such clones already increased after a single lyophilization of the strain. Among the total number of resistant strains 5 were selected which exhibited the greatest resistance to repeated lyophilization. The results of study of the immunogenicity of vaccines prepared on the basis of the selected strains and clones are represented in Table 3.

Table 3 shows that the experimental series of the vaccine retained their immunogenic properties.

Table 3. Immunogenic properties of vaccine prepared on basis of selected strains

	Immunogenicity Im D_{50}	
Vaccine series	for white mice	for guinea pigs
Initial strain (control)	11,170 (8,102-18,620)	5,792 (1,990-10,000)
Singly lyophilized strain	145,000 (6,481-32,410)	4,898 (1,896-9,989)
Doubly lyophilized strain	7,254 (3,244-16,220)	7,634 (3,425-18,032)
Clone 14	1,903 (851-4,256)	
Clone 20	6,467 (3,398-10,000	
Clone 21	3,803 (1,700-8,506	
Clone 37	637 (334-1,674)	
Clone 38	2,130 (952-4,762	

One of the most immunogenic clones 37 was selected for further selection for the purpose of strengthening the property of resistance to lyophilization. A subclone 37/28, still more resistant to lyophilization, was obtained from its population, and from the population of this subclone — the subclone 37/28/20, and from the latter — 37/28/20/5. The viability of the cells of the selected clone in the experimental series of the vaccine exceeded the corresponding index for the initial strain by a factor of 2 or more and was 47.2+/-5.8 versus 21.3+/-4.1 colony forming units.

Table 4. Indices of thermal stability of experimental series of live dry plague vaccine and their predicted storage times

Vaccine series	Thermal stability index*, days	Predicted vaccine storage time at 4°, years
Initial strain	4.08	3.6
Singly lyophilized strain	9.04	4.3
Doubly lyophilized strain	13.2	7.3
Selected clone 37/28/20/5	14.4	8.3

*50 percent decrease in viability at 37°.

The vaccines prepared on the basis of the selected strains and clones differed from the initial vaccines not only with respect to the degree of viability, but also with respect to thermal stability (Table 4).

The data cited in Table 4 indicate a considerable increase in the thermal stability of vaccines prepared on the basis of selected strains. The thermal stability index of these vaccines exceeds the corresponding index for the control series by a factor of 2-3. The predicted storage times of these vaccine series are increased. The high thermal stability of the vaccine developed on the basis of strains resistant to lyophilization favor the retention of its efficacy under unfavorable transport and storage conditions.

The strain whose genome contains a plasmid resistant to antibacterial agents retained its properties after single and double lyophilization. Thus, the multiple lyophilization and selection of strains method at the clone level made it possible to obtain lyophilization-resistant strains having a high thermal stability and immunogenicity. The proposed experimental approaches can be used for stabilizing the cell makeup of vaccine strains of the plague microbe and on their basis the development of effective vaccines with an increased shelf life.

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Purification and Some Properties of Protease of Plague Microbe

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[Article by S. P. Yevlakhova and B. N. Mishankin; Antiplague Scientific Research Institute, Rostov-na-Donu; the first paragraph is an abstract; UDC 579.842.23:577.15]

[FBIS Translated Text] A protease with a molecular weight of the monomer 36 kDa (according to SDS-PAAG electrophoresis data) was isolated from Yersinia pestis EV 76 cells with use of chromatography on DE-52 and hydroxylapatite and also with gel filtration on G-200. The enzyme was completely inhibited by phenylmethylsulfonylfluoride and tosyl-lysine chlormethylketone, partially inactivated with EDTA and phenanthroline, but not inactivated with thimerosal and p-chlormercuribenzoate. The trypsin-like protease was capable of hydrolyzing peptides containing arginine and alkaline proteins (histone, protamine), but not albumin and casein.

Purified proteolytic enzymes with a known substrate specificity are attracting attention because they can be used in a study of the fine structure of different protein molecules, as drugs and in the food and pharmaceutical industry [1, 2]. For a long time the presence of active proteases in the plague microbe remained in question [3]. We were able to show the presence in an extract of the plague microbe of peptidases capable of hydrolyzing biologically active peptides: the human immunogenic peptide taphtsin, opioidal peptide leu-enkephalin, vasoactive peptides angiotensin and bradykinin, as well as synthetic substrates typical for different proteases and peptidases, were subjected to proteolytic degradation [4].

The purpose of the study was purification of the protease of the plague microbe and study of its substrate spectrum and some physicochemical properties.

Experimental Conditions

Bacteria of the vaccine strain Y. pestis EV 76 were cultivated on Hottinger's agar at 28° for 48 hours. Then they were washed with a 10 mM tris-HCl-buffer, pH 8.0. The cell mass was collected by centrifuging (Beckman, United States, rotor A-10) for 8,000 min^{-1}. The cells suspended in this same buffer were processed in a disintegrator (MSE, Great Britain) for 6 minutes with a one-minute pause for cooling each 30 s. All the operations were performed at 4°.

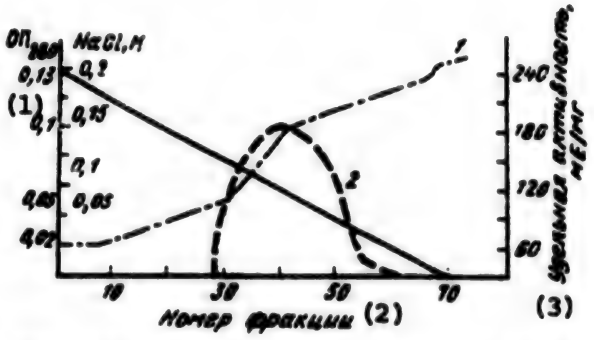

Fig. 1. Chromatography of proteins of cell extract of plague microbe on DE-52 cellulose: 1 — optical density at λ 280 nm; 2 — specific activity of enzyme, IU/mg.

Key: 1. Optical density. 2. Number of fraction. 3. Specific activity, IU/mg

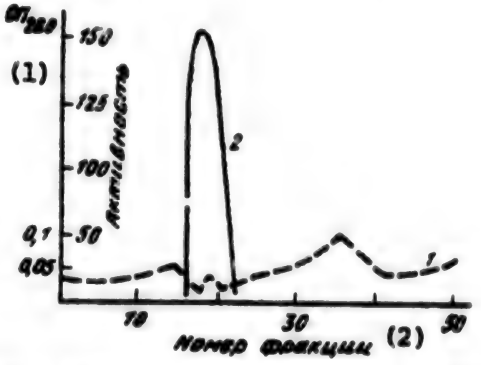

Fig. 2. Elution profile of a preparation of plague bacteria during gel filtration through a Sephadex G-200 column: 1 — optical density at λ 280 nm; 2 — activity of the enzyme

The protein was determined by the Warburg method. In a graphic representation of the processes of chromatographic separation of proteins use was made of nominal absorption units at λ = 280 nm. A nationally produced SF-16 spectrophotometer (Lomo, St. Petersburg) was used in the work.

Table 1. Isolation and purification of trypsin-like protease from cells of Y. pestis EV 76

Purification stage	Total protein, mg	Total activity, IU	Specific activity, IU/mg of protein	Purification, times
Cell extract	6,705	5,999,634	894.8	1
DE-52 chromatography	145.98	2,157,442	14,779	16.5
HAP chromatography	90	1,078,721	11,985.78	13.4
G-200 gel filtration	6.37	341,730	53,646	60

The protease activity was determined from the hydrolysis of benzoylarginine ethyl ester (BAEE). The incubation mixture contained 0.5 ml of the substrate (1 mg/ml of tris-HCl buffer, pH 8.0), 0.1 ml of the enzyme and 2.4 ml of the same buffer.

The optical density was measured at λ 253 nm before and after 15-minute incubation at 37°. The employed activity unit was the quantity of the enzyme hydrolyzing 1 μmol BAEE/1 mg of preparation per minute.

Table 2. Influence of temperature on activity of trypsin-like protease of Y. pestis EV 76

Processing of sample	Residual activity	
	IU	%
Control (without processing)	39.842	100
50°, 10 min	42.550	81
75°, 10 min	9.055	22.7
100°, 1 min	0	0

The hydrolysis of casein, albumin, protamine and histone (Serva, FRG) was in 0.1 M tris-HCl-buffer, pH 8.0 for 3 hours at 37°. The degree of hydrolysis was judged from the quantity of arginine in the hydrolysis products soluble in trichloracetic acid (TCAA) by the Sakaguchi method [5].

Electrophoresis was carried out using a Bio-Rad instrument (United States) in vertical plates with a thickness of 7 mm in PAAG by the Laemmli method [6]. Bovine serum albumin (67 kDa), ovalbumin (43 kDa), carboxylase (31 kDa) and a soy inhibitor of trypsin (21 kDa) were used as marker proteins for determining molecular weight.

Tris-HCl and K,Na phosphate buffer systems in the range of pH values from 6.0 to 9.0 were used in determining the optimum of the pH effect of the enzyme. The resistance of the enzyme to a high temperature was judged from its residual activity after first being held at 50°, 75° and 100°.

Table 3. Effect of inhibitors and ions of metals on activity of protease of Y. pestis EV 76

Reagents	Concentration, mM	Residual activity, %
Phenylmethylsulfonylfluoride	1	0
Tosyl-lysine chlormethylketone	0.25	0
p-Chlormercuribenzoate	1	100
Thimerosal	1	12.1
Phenanthroline	1	40
EDTA	1	40
Zn^{2+}	1	0
Ni^{2+}	1	0
Cu^{2+}	1	0
Co^{2+}	1	0

The inhibiting effect on the enzyme was studied by its preincubation at 37° for 1 hour with one of the following substances: phenylmethylsulfonylfluoride, p-chlormercuribenzoate, pepstatin, EDTA, phenanthroline, thimerosal, tosyl-lysine chlormethylketone, as well as ions of metals in a concentration 1 x 10^{-3} M (Sigma, Serva, FRG). Sephadex G-200, cellulose (KM, DE-52) and hydroxylapatite (HAP) of the Serva Company were used for the chromatographic separation of proteins.

Results and Discussion

Chromatography with DE cellulose. Weak cation- and anion exchangers are usually used for ion exchange chromatography of proteins because the proteins are represented by multiple ions capable of binding strongly with the carrier. The testing of the investigated protein with protease activity from an extract of cells of the plague microbe indicated that KM cellulose does not ensure its binding in any of the proposed tris- or phosphate buffers, whereas cellulose DE-52 quite solidly held the enzyme introduced into both 10 mM tris-HCl and a K,Na phosphate buffer, pH 6.7. Thus, binding with a weak cation exchanger, the investigated protein with proteolytic activity manifested its alkaline properties.

Table 4. Hydrolysis of protein substrates of protease from Y. pestis EV 76

Substrate*	Activity, μg arg/ml
Casein	0
Albumin	0
Protamine	19
Histone	12

*Concentration — 10 mg/ml.

In a standard experiment the proteins of the extract from the cells of the plague microbe in a quantity 6.705 mg were introduced into a column with DE-52 cellulose (3 x 10 cm), balanced with a 10 mM tris-HCl-buffer, pH 8.0. The elutriation of the proteins was with the same buffer with the addition of NaCl. First the column was washed free of proteins, eluting from the column 0.1 M NaCl, followed by chromatographic separation with a linear gradient of the NaCl concentration (0.1-0.2 M). The BAEE-hydrolyzing activity and the protein

concentration were determined in each fraction. It was found that the active fraction is eluted with 0.15 M NaCl (Fig. 1). The degree of purification was determined from the change in the specific enzymatic activity (Table 1). HAP chromatography. Chromatography in a column with HAP assumes the introduction of the preparation in a buffer with a weak concentration with a subsequent separation of the proteins with an increase in the molarity of the phosphate buffer, competing with the proteins of the preparation with respect to the degree of binding with the carrier [7]. The combined enzymatic preparation was not sorbed on the HAP in the phosphate buffer, but was bound with the carrier after dissolution in 10 mM tris-HCl buffer, pH 8.0, even in the presence of 150 mM NaCl. It was found that even with the lowest concentrations of the phosphate buffer the enzyme was removed from the carrier, which we then used for chromatography. And although the efficiency of this procedure in general was low (see Table 1), it was included in the purification model for concentration of the enzyme. The monitoring of purity of the preparation using electrophoresis indicated that the preparation after elutriation with HAP nevertheless was represented by several protein components.

Gel filtration on G-200. The final stage in enzyme purification was gel filtration of the preparation concentrated after HAP chromatography. The protein preparation (90 mg) in a volume 1 ml was introduced into a column with G-200 (1.5 x 100 cm), balanced with a 10 mM phosphate buffer, pH 6.7, with subsequent elutriation with the same buffer. Figure 2 shows the profile of preparation elutriation.

The monitoring of the collected enzyme by means of PAAG electrophoresis under denaturizing conditions with 0.1 percent SDS revealed the presence of a single band of protein with a molecular weight 36 kDa (Fig. 3). The determination of the molecular weight of native protein by means of gel filtration in a column with G-200 gave a value 75 kDa, which was twice as great as the results obtained by electrophoresis. In our opinion this fact supports a dimer structure of the enzyme.

Taking into account the quite high specificity of the reaction of determination of the activity of the enzyme, for study of some of its physicochemical properties use was made of the partially purified preparation after chromatography with DE-52 cellulose.

The hydrolysis reaction took place in two buffer systems, tris-HCl and K,Na-phosphate, in the range of pH values from 6.0 to 9.0. The optimum pH values for BAEE and BAHA hydrolysis coincided and corresponded to 8.0 (Fig. 4).

The data in Table 2 show that the enzyme does not fall in the class of thermally stable proteins. Its boiling for 1 min reduced the activity by a factor of more than 10, whereas 10-minute preincubation at 50-75° decreased the activity of the enzyme by 20-80 percent, which is evidence of its quite solid structure.

An inhibitor analysis revealed a high sensitivity of the enzyme to group-specific inhibitors of serine proteinases — phenylmethylsulfonylfluoride and an inhibitor of trypsin — tosyl-lysine chlormethylketone, which indicates that it belongs to the trypsin-like proteases (Table 3).

The activity of the enzyme did not change with exposure to inhibitors of thiol proteinases — p-chlormercuribenzoate and thimerosal. Chelate-forming compounds — phenanthroline and EDTA, in this case serving as inhibitors of metalloproteinases, reduced enzymatic activity by 60-90 percent. It was found that ions of the metals Zn^{2+}, Ni^{2+}, Cu^{2+} and Co^{2+} completely inhibited enzymatic activity, but Ba^{2+} ions reduced it by 56 percent. Ca^{2+} and Mg^{2+} ions exerted no influence on the enzyme.

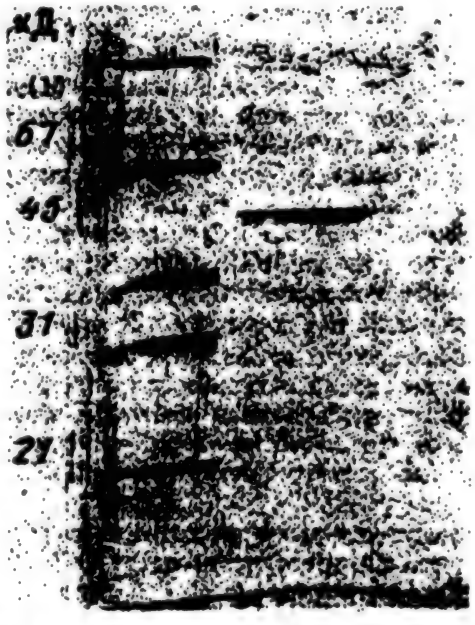

Fig. 3. Electrophoregram of protease of plague microbe in 7.5 percent PAAG with 0.1 percent SDS with marker proteins: bovine serum albumin (67 kDa), ovalbumin (43 kDa), carboxylase (31 kDa), soy inhibitor of trypsin (21 kDa).

Key: 1. kDa

As noted above, an extract from cells of the plague microbe is capable of hydrolyzing biologically active peptides. The trypsin-like protease which we isolated, hydrolyzing the synthetic peptides BAEE and BAHA, which we isolated, manifested the properties of peptidase and therefore was additionally characterized by a capacity for splitting protein substrates. The enzyme purified to a homogeneous state did not hydrolyze casein and albumin to products soluble in TCAA. However, the arginine-rich alkaline proteins histone and protamine proved to be sensitive to the influence of the trypsin-like enzyme isolated from plague microbe cells (Table 4).

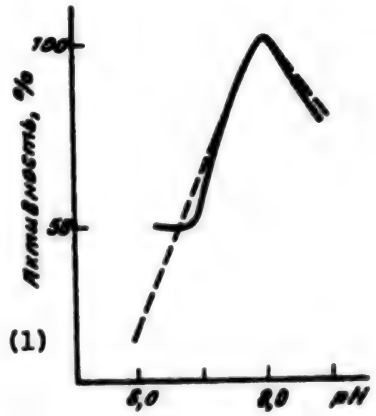

Fig. 4. Influence of pH on activity of protease of plague microbe when using BAEE and BAHA as substrates.

Key: 1. Activity, %

Thus, a trypsin-like enzyme, capable of hydrolyzing peptides and alkaline proteins, was isolated, purified and partially characterized. And although its importance for the biology of the causative agent of the plague in many respects for the time being remains unclear, the very fact of the existence of intracellular protease with a singular substrate spectrum makes it possible with great assurance to speak of the possibility of the transpiring of processes of cell autodegradation of protein in different physiological states (aging, stress, etc.).

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Influenza: State of the Problem and Current Epidemiological Situation

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[FBIS Translated Text] Influenza and other acute respiratory diseases of virus etiology remain uncontrollable infections, on the one hand, owing to the high variability in the antigenic structure of circulating influenza viruses and, on the other, owing to the high heterogeneity of the group of viruses of acute respiratory diseases, which number more than 200 various types of causative agents. It is difficult to overestimate the damage done to the population's health by influenza and its complications. According to WHO reports, about 5 million children under the age of 5 annually die from acute respiratory diseases and pneumonia. The highest mortality due to influenza is among individuals over the age of 60.

It should be especially stressed that the existing ideas of influenza as an acute self-sterilizing infection by no means exhaust the entire diversity of clinical forms of the disease. The results of research on the modeling of influenza infection on laboratory animals and clinical observations indicate that influenza viruses, like other causative agents, for example, from the group of paramyxoviruses, under certain conditions can persist in the organism for a long time [1-7, 13, 14].

The mechanisms of many delayed sequelae of influenza infection, including chronic pneumonias, bronchites [13,

14], myocardites [9, 12, 15, 17, 18], nephropathies [19], postinfluenza encephalopathies [8, 10, 11, 16], and intrauterine pathology of the fetus, have not been clarified up to now.

Problems concerning the contribution of viruses of influenza and of other acute respiratory diseases, which cause mass infectious diseases, to the development of diseases of an autoimmune nature, including diabetes mellitus, remain unsolved, although the first reports on the modeling of this disease on transgenic mice with the expression of the hemagglutinin of the influenza virus have appeared. The possibility of induction of diabetes mellitus of an autoimmune nature by the hemagglutinin of the influenza virus can be connected with the phenomenon of molecular mimicry, that is, with the presence of common antigenic determinants in virus proteins and membrane proteins of cells of Langerhans islets. At the same time, acute respiratory diseases as mass infections during the period of epidemics greatly deform immunity and, causing an active production of lymphokines, can lead to lymphoproliferative and autoimmune processes involving other tissues. For example, workers at the Institute of Influenza of the Russian Academy of Medical Sciences established the appearance of brain tissue antibodies in patients who had influenza during the 1975-1982 period.

Thus, data on the fact that influenza and acute respiratory diseases have a significant effect on the formation of the background for postinfectious somatic morbidity among the population have been accumulated in the last few years. This fact in no way was taken into consideration during the vaccinal prevention and treatment of influenza and acute respiratory diseases.

In developed countries throughout the world under WHO auspices a constant supervision of the circulation of the causative agent is carried out, problems of genome evolution are studied, and a search is conducted in the area of development of improved preparations of influenza vaccines, chemical preparations, means and methods of specific diagnosis, and new approaches to the production of pathogenetic therapy agents. In Russia the Federal Center of Influenza, which interacts with 39 Russian support bases and 20 bases located in the territory of CIS countries and Baltic states, performs the functions of supervision of influenza.

This issue of the journal presents the latest work of the Scientific Research Institute of Influenza of the Russian Academy of Medical Sciences and other institutions, which contains the most recent data on the epidemiology and supervision of influenza and acute respiratory diseases and information on the development of new approaches to the creation of specific means and methods of antivirus therapy and of the diagnosis and prevention of respiratory virus infections.

This article presents materials describing the development of the latest epidemic events in Russia and other countries throughout the world in 1993-1994.

Countries of Western Europe

The first local outbreaks of influenza were recorded in Great Britain (Scotland) among university students as far back as September-October 1993. An increase in influenza-like diseases among the population began in October and the peak of morbidity was noted in Wales during the first week of November and in Scotland and England a week later. Its level was the highest in Scotland. Mortality due to influenza and pneumonias exceeded threshold values in November and during the first half of December and a repeated rise in mortality was observed in the second half of January.

After Great Britain the epidemic process gripped France, where the rise in morbidity, which began in November, ended in a peak recorded during the first week of December. During the second week of December the morbidity peak was also observed in Belgium, Denmark, the Netherlands, and Norway, during the third week, in Austria, Finland, and Sweden, and during the fourth week, in Switzerland (Table 1). In a number of countries the epidemic was characterized by a high intensity. For example, in Denmark the highest morbidity level was recorded in the last 25 years (from 1969) and in Norway, 19 years (from 1975). In Switzerland and Sweden from 5 to 15 percent of the population was sick. In Scotland the morbidity level reached 120 per 10,000 people.

Table 1. Development of Influenza Epidemic in 1993-1994 (Morbidity Peak) in Various Countries Throughout the World

Month	Week	Country
1993		
November	First	Wales
	Second	Scotland, England
	Third	—
	Fourth	—
December	First	France
	Second	Belgium, Denmark, Netherlands, Norway
	Third	Austria, Finland, Sweden
	Fourth	Switzerland
1994		
January	First	United States
	Second	
	Third	
	Fourth	Bulgaria, Czechoslovakia, Hungary, Rumania, Uzbekistan
February	First	
	Second	Lithuania
	Third	Russian Federation
	Fourth	Belarus

Countries of Eastern Europe

The epidemic rise in morbidity began only in January with a peak during the fourth week of the month noted almost simultaneously in Bulgaria, Czechoslovakia, Hungary, and Rumania.

Etiology of epidemics. Everywhere in countries of Western and then Eastern Europe the epidemic process was caused by influenza A (H3N2) viruses antigenically related to the A/Peking/32/92 reference strain. Epidemic strains were characterized by some biological properties. They were better isolated on the MDCK cell culture than on chick embryos and agglutinated erythrocytes of guinea pigs severalfold more strongly as compared with commonly used chick erythrocytes. In individual cases influenza B viruses were isolated in the Netherlands, Sweden, Switzerland, and England.

United States

The first reports on unusually early local outbreaks of influenza A (H3N2) in the middle of August-beginning of September 1993 were received from CDC (Atlanta). A marked rise in influenza-like diseases among the population etiologically connected, as in European countries, with influenza A (H3N2) viruses antigenically related to the strain A/Peking/32/92 began in the second half of November. An excess of epidemic thresholds of mortality due to influenza and pneumonias was recorded from the middle of December. At the beginning of January, when morbidity due to influenza and acute respiratory diseases reached the peak and its proportion made up 5 to 8 percent in the structure of the general morbidity, mortality due to influenza and pneumonias reached the highest values in recent years (9.3 percent in the structure of general mortality). A decline in morbidity began in February, but it was noted sporadically in 14 states through the third week in March, when the proportion of influenza-like diseases dropped to 1 percent.

During the epidemic period in the United States more than 4,000 strains of the influenza A virus were isolated, among which influenza A (H3N2) viruses made up 99 percent and influenza A (H1N1) viruses, 1 percent.

There were also individual reports on the isolation of influenza B viruses antigenically related to the strain B/Panama/45/90. The index of virus isolability made up about 14 percent (of the number of those examined).

Countries of South-Eastern Asia

In contrast to countries of America and Europe, where the influenza A (H3N2) virus was the main causative agent of the epidemic, reports arriving from China, Hong Kong, and Thailand point to a preferential isolation of influenza B viruses.

In Japan, in contrast to these countries, right up to the middle of February a very low level of influenza morbidity was noted. Among the isolated causative agents influenza A (H3N2) viruses dominated, while influenza B viruses were isolated only in individual cases (43 and 3 strains respectively).

Southern Hemisphere

According to WHO information, in individual regions of the southern hemisphere during the summer period of 1993 a certain rise in morbidity due to influenza-like infections was noted, in particular in the second half of July in Madagascar, where the influenza A (H3N2) virus was isolated as long ago as April 1993. Influenza A and B began to be diagnosed in Australia in the vicinity of Melbourne from the beginning of June. Influenza A was confirmed in a number of cities in the State of Victoria. In August morbidity due to influenza and acute respiratory diseases and the frequency of virus isolation increased, but morbidity was below the epidemic threshold. Influenza A (H3N2) and B viruses were isolated from patients. In July-August an increase in morbidity was noted in New Zealand, where influenza A (H3N2) and B viruses were also isolated. Influenza A (H3N2) viruses were isolated in South Africa (Johannesburg and Randfontein) and Zambia (Lusaka) in June and several large local outbreaks of influenza A (H3N2) were noted in Zambia in June-September.

Russian Federation and CIS Countries

According to official data of the Federal Center of Influenza and Acute Respiratory Diseases (FTsG)[1], morbidity remained at a low level (18-57 per 10,000 of the population) right up to the second 10-day period of January, when in most (71 percent) of Russia's cities a distinct rise in influenza-like diseases began.

For the first time an excess of epidemic thresholds was noted during the last week of January in 3 out of 37 cities, which sent reports to the FTsG (Arkhangelsk, Barnaul, and Tashkent), the morbidity level in them ranging from 93 to 102 per 10,000 of the population (tables 2 and 3). The following week (31 January through 2 February 1994) the epidemic threshold was reached in another seven cities (Vilnyus, Yekaterinburg, Karaganda, Minsk, Omsk, Ufa, and Chelyabinsk). The morbidity level was the highest in Arkhangelsk, Barnaul, Minsk, and Chelyabinsk (162, 150, 148, and 127 per 10,000 of the population respectively).

Table 2. Characteristics of the 1994 Influenza Epidemic

City	Length of Epidemic, weeks	Peak Time, week	Peak Value		Morbidity, %								
			with background of acute respiratory diseases	without background	due to influenza and acute respiratory diseases			Overall illnesses		Total	due to influenza		Total
					0-2 years	3-6 years	7-14 years	0-14 years	15 years and older		0-7 years	7 years and older	
Arkhangelsk	6	3d	1.9	1.1	16.0	23.3	16.8	18.3	5.9	8.5	5.6	3.3	4.0
Astrakhan	4	3d	1.1	0.6	11.2	13.4	8.2	10.0	2.6	3.9	5.1	1.3	2.0
Alma-Ata	1	1st	0.9	0.1	2.2	2.6	1.6	2.0	0.6	0.9	-	-	0.2
Barnaul	5	3d	2.0	1.3	14.1	18.1	13.3	15.2	5.1	7.3	4.8	2.6	4.3
Vilnyus	5	2d	1.6	1.0	21.7	16.3	16.6	17.5	3.6	6.5	7.0	1.6	3.7

City	Length of Epidemic, weeks	Peak Time, week	Peak Value		Morbidity, %							
			with background of acute respiratory diseases	without background	due to influenza and acute respiratory diseases			Overall illnesses		Total	due to influenza		Total
					0-2 years	3-6 years	7-14 years	0-14 years	15 years and older		0-7 years	7 years and older	
Vladivostok	2	2d	0.7	0.2	-	-	-	-	-	1.3	-	-	0.2
Volgograd	4	2d	1.4	0.7	9.6	12.7	9.5	10.4	2.8	4.2	2.6	0.8	1.0
Voronezh	3	3d	1.6	0.8	9.5	10.7	8.8	9.5	3.1	4.4	3.4	1.5	2.2
Dnepropetrovsk	3	1st	1.6	0.7	9.9	12.9	8.0	9.6	3.0	4.3	2.9	1.7	1.8
Yekaterinburg	3	2d	1.2	0.5	7.3	6.9	5.2	5.8	2.0	3.1	1.1	0.4	0.9
Irkutsk	2	1st	1.0	0.3	6.2	6.3	3.3	4.6	1.2	1.8	0.7	0.5	0.5
Kazan	3	1st	0.9	0.3	6.9	7.1	4.6	4.8	1.9	2.7	0.5	0.7	0.7
Kaliningrad	3	3d	1.2	0.5	10.6	8.3	8.2	8.6	1.9	3.2	2.4	0.8	1.2
Karaganda	3	2d>	1.1	0.4	8.6	9.0	5.4	7.5	1.8	3.1	2.2	0.8	1.1
Kemerovo	3	1st	1.7	0.8	9.1	11.5	10.3	10.4	2.9	4.6	1.1	2.2	2.1
Kiev	2	1st	1.7	0.4	8.8	7.7	5.5	6.4	2.3	3.2	0.8	0.4	0.7
Kirov	3	2d	1.6	0.8	9.8	11.3	9.0	9.7	3.2	4.5	1.7	1.4	1.9
Krasnodar	1	1st	1.0	0.3	3.3	2.3	1.3	1.9	0.7	1.0	0.5	0.1	0.3
Lvov	1	1st	1.4	0.4	7.9	2.6	3.2	3.6	1.0	1.4	2.5	0.2	0.4
Minsk	5	4th	2.4	1.3	20.9	23.2	15.1	20.4	7.4	9.6	5.3	4.0	4.2
Moscow	1	1st	1.4	0.2	4.1	3.7	2.9	3.3	0.9	1.4	-	0.1	0.2
Nizhniy Novgorod	4	3d	1.8	0.9	15.8	16.6	12.8	14.3	4.7	6.7	3.6	2.2	3.3
Omsk	5	3d	1.9	1.2	17.5	20.5	15.0	16.7	3.9	6.3	5.7	1.6	2.7
Perm	4	2d	1.3	0.5	9.0	11.6	7.3	8.7	3.2	4.4	0.8	1.4	1.4
Rostov-on-Don	3	2d	1.2	0.5	16.1	8.9	6.6	8.2	2.0	3.2	4.2	0.4	0.1
Samara	4	2d	1.3	0.5	13.3	13.9	10.2	11.4	3.5	5.0	2.6	0.9	1.6
Saratov	3	1st	1.8	1.01	1.3	14.6	9.3	11.1	3.4	4.8	2.7	1.6	2.4
Simferopol	2	1st	0.8	0.2	-	-	-	-	-	1.6	-	-	0.4
Smolensk	3	3d	1.6	0.5	15.5	13.6	6.8	10.0	3.1	4.4	2.0	1.0	1.3

City	Length of Epidemic, weeks	Peak Time, week	Peak Value		Morbidity, %								
			with background of acute respiratory diseases	without background	due to influenza and acute respiratory diseases			Overall illnesses		Total	due to influenza		Total
					0-2 years	3-6 years	7-14 years	0-14 years	15 years and older		0-7 years	7 years and older	
Stavropol	1	1st	1.0	0.3	3.8	4.4	2.9	3.5	0.4	1.0	0.9	-	0.3
Tashkent	2	1st	1.0	0.4	5.4	4.9	3.1	4.0	1.2	2.0	1.6	0.3	0.8
Ufa	5	3d	1.2	0.71	3.0	15.4	9.4	12.0	3.5	5.0	5.8	1.8	2.5
Ulan-Ude	1	1st	0.9	0.2	3.2	2.4	1.4	2.0	0.5	0.9	-	-	-
Khabarovsk	2	1st	1.0	0.3	6.6	7.4	4.4	5.6	1.0	2.0	2.0	0.2	0.6
Chelyabinsk	3	2d	1.9	0.9	9.7	12.0	7.2	9.0	3.3	4.8	1.6	2.2	1.9
Chita	2	1st	1.0	0.3	8.2	7.5	4.2	5.6	0.8	1.9	-	-	0.4
Yuzhno-Sakhalinsk	3	1st	1.1	0.4	4.2	10.5	5.4	6.6	1.6	2.7	-	-	0.5
Yakutsk	5	3d	1.3	0.8	13.4	19.1	8.1	12.1	2.4	4.9	-	-	2.2
On the average	2.9	1.7	1.3	0.6	10.1	10.9	7.5	8.9	2.6	3.8	2.8	1.4	1.5

Remark. Dash—there are no data.

During the second week of February the epidemic gripped 12 (28.5 percent) of 42 cities. The highest morbidity level was noted in the same cities (175-197 per 10,000). During the third week of February (from 14 through 20 February 1994) the epidemic threshold of morbidity was reached in more than one-half of the cities (in 22 out of 41), including for the first time in Voronezh, Dnepropetrovsk, Irkutsk, Kazan, Kaliningrad, Kemerovo, Kirov, Moscow, Rostov-on-Don, Samara, Smolensk, and Chita. As before, the highest morbidity level was recorded in cities that were first gripped by the epidemic process (Arkhangelsk, Barnaul, and Minsk), as well as in Omsk (174-229 per 10,000 of the population).

During the last week of February-first week of March the epidemic gripped 57 and 58.3 percent of the cities respectively. However, in some regions a tendency toward a decrease in morbidity began to show. As a result, during the second week of March (from 7 through 14 March 1994) an excess of the epidemic threshold of morbidity was recorded only in two cities (Yakutsk and Volgograd) and the morbidity level as a whole did not exceed 104 to 106 per 10,000. From 14 through 20 March 1994 a synchronous short-term rise in morbidity (of 10 to 81 percent) was noted in most cities, as a result of which epidemic thresholds were again exceeded in Astrakhan, Volgograd, Minsk, Magadan, and Stavropol. An epidemic rise in morbidity continued in Yakutsk. During the last week of March and during the first week of April a general pronounced decrease in morbidity occurred. As a result, at the beginning of April the situation with respect to influenza, on the whole, was normalized, excluding Yakutsk, where morbidity exceeded the epidemic threshold.

Thus, the epidemic, which began during the last week of January, reached the peak during the second half of February-first week of March (7th to 9th week of the year) with a marked decline during subsequent weeks of March and normalization of the situation by the beginning of April (excluding Yakutsk, which was the last to join the epidemic process).

Table 3. Development of the 1994 Influenza Epidemic by Regions

Region	City	Data									
		30 January	6	13	20	27	6	13	20	27	5
			February				March				April
Europe:											
North-West	Arkhangelsk	e	e	p	e	e	e				
West	Vilnyus		e	p	e	e	e				
	Lvov					p					
	Kalin-ingrad				e	e	p				
	Minsk		e	e	e	p	e	-	e		
Center	Moscow				p						
	Voronezh				e	e	p				
	Smolensk				e	e	p				
	Kiev					p	e				
Volga Region	Nizhniy Novgorod			e	e	p	e				
	Kazan				p	e	e				
	Saratov				p	e	e				
	Samara			e	p	e	e	-	e		
	Astrakhan			e	p	e	-	-	e		
	Vol-gograd					e	p	e	e		
Urals and the Ural Region	Perm			e	p	e	e				
	Ufa		e	e	p	e	e				
	Kirov				e	p	e				
	Yekater-inburg		e	p	e						
	Chelyabinsk		e	p	e						
South	Dne-propetro-vsk				p	e	e				
	Stavropol						p		e		
	Rostov-on-Don				e	p	e				

Region	City	Data									
		30 January	6	13	20	27	6	13	20	27	5
			February				March				April
	Krasnodar						p				
	Simferopol				p	e					
Asia:											
Siberia	Irkutsk				p	e					
	Kemerovo				p	e	e				
	Omsk		e	e	p	e	e				
	Chita				p	e					
	Karaganda		e	p	e						
	Barnaul	e	e	p	e	e					
	Ulan-Ude						p				
Central Asia:	Tashkent	p	e								
	Alma-Ata						p				
Far East:	Khabarovsk					p	e				
	Vladivostok					e	p				
	Yuzhno-Sakhalinsk				p	e	e				
Far North	Magadan								e		
	Yakutsk							e	e	p	e

Remark: e — epidemic week; p — epidemic peak.

During the epidemic period morbidity in Arkhangelsk, Barnaul, Minsk, and Nizhniy Novgorod, where 8.5, 7.3, 10, and 6.7 percent of the people fell sick, was the highest and the length of the epidemic was 4 to 6 weeks.

During the epidemic period 4 to 5 percent of the population fell sick in Voronezh, Dnepropetrovsk, Kirov, Perm, Samara, Smolensk, and Chelyabinsk, 2 to 3.9 percent, in Astrakhan, Kazan, Kaliningrad, Rostov-on-Don, Tashkent, and Khabarovsk, and less than 2 percent of the population, in Irkutsk, Lvov, Moscow, Ulan-Ude, and Chita. Among children morbidity due to influenza and acute respiratory diseases was noted two- to three-fold more frequently than among adults.

Etiology of the epidemic. Judging by the limited data on the isolation of viruses, the influenza A (H3N2) virus (13 strains were isolated) was the main causative agent of the epidemic in the European part of the Russian Federation and CIS countries (Astrakhan, Vilnyus, and Moscow), while influenza B viruses (23 strains) were isolated mainly in the Far East (Khabarovsk and Vladivostok), as well as in countries of South-East Asia. A report on the isolation of influenza A (H1N1) viruses came from Stavropol (Table 4).

Table 4. Results of Isolation of Influenza Viruses in the Country's Various Regions During the Period From 28 June 1993 Through 17 April 1994

City	A (H1N1)					A (H3N2)					B				
	total	days of the week				total	days of the week				total	days of the week			
		0-2	3-14	15-30	30		0-2	3-14	15-30	30		0-2	3-14	15-30	30
Astrakhan						3		3							
Vilnyus						4	1	3							
Vladivostok											1		1		
Kemerovo											1			1	
Stavropol	1				1										
Ulan-Ude						3		3							
Khabarovsk						3	2		1		21	8	7	5	1
Total	1				1	13	3	9	1		23	8	8	6	1

Viruses were isolated primarily from children, among whom everywhere the morbidity level was 2- to 3.6-fold higher than among the entire population.

Most of influenza A (H3N2) viruses isolated during the 1994 epidemic were drift-variants of the A/Peking/32/92 reference strain. However, strains related to the new A/Shangdong/9/93 reference strain were also detected among the isolates of this epidemic season. It must be noted that individual viruses with a similar specificity of hemagglutinin were also isolated during the 1992-1993 epidemic season. Serologic analysis data also pointed in favor of the primary circulation of influenza A (H3N2) viruses. According to the hemagglutination-inhibition test data, during the period of the rise in morbidity the proportion of influenza A (H3N2) diseases reached 32 to 78 percent in the structure of acute respiratory diseases in cities of the European part of Russia, the Volga Region, and West Siberia.

Diseases connected with influenza B were recorded with a high frequency (25 to 35.3 percent) in Khabarovsk, where influenza A (H3N2) viruses also circulated simultaneously (in 11.8 to 40.9 percent of the cases).

Thus, the 1993-1994 influenza epidemic connected with the circulation of viruses similar to the strain A/Peking/32/92 (H3N2) began in countries of North America and Western Europe in October-November and moved to countries of Eastern Europe and to the territory of the Urals and West Siberia. In China and in the Far East epidemic events were connected mainly with influenza B viruses.

Influenza A (H1N1) viruses did not become widespread. Individual isolates (according to the data of CDC, Atlanta, United States, about 1 percent of the total isolated viruses) caused only sporadic morbidity in some cities. This makes it possible to assume the possibility of a conclusion of the 14-year period (1977-1991) of epidemic activity of influenza A (H1N1) viruses.

The last influenza A (H3N2) epidemic in the Russian Federation was characterized by a moderate intensity. Although morbidity involved all population groups, primarily children were affected.

In Russia's territory the highest morbidity indices were recorded in Arkhangelsk, Barnaul, Nizhniy Novgorod, Omsk, Samara, and Smolensk, where during the epidemic period about 16 to 18 percent of the children under the age of 14 and 3.5 to 5.9 percent of the population 15 years old and above fell sick.

High morbidity indices were also recorded in Minsk and Vilnyus.

Footnotes

1. Yu.V. Lukyanov, Ye.Z. Parsagashvili, A.O. Zhukov, A.G. Onufriyev, and Yu.G. Ivannikov participated in the preparation of FTsG materials.

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Some Characteristics of Circulation of Respiratory Viruses in the Country's Territory

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[Article by A.K. Golovanova and T.I. Yurlova, St. Petersburg Scientific Research Institute of Influenza of the Russian Academy of Medical SciencesUDC 616.98:578.831.31-036.2.07]

[FBIS Translated Text] Respiratory virus infections in their proportion occupy one of the first places in the structure of man's infectious pathology. In our country's territory, on the average, more than 60 million people annually have the indicated diseases. In connection with this problems concerning the study of present-day etiology of respiratory virus infections acquire decisive importance both for our country and for a number of countries throughout the world [1-4.8].

For a successful etiotropic treatment and prevention of acute respiratory diseases in people, first of all, it is necessary to detect epidemically current viruses for the country's different regions and to establish their change in different territories and spread during different seasons of the year and in different age population groups.

The existing antigenic and genetic heterogeneity of respiratory viruses and different epidemiological potentials of circulating variants of these causative agents make a continuous observation of their spread justified.

Taking this into consideration, WHO proposed a wide program for scientific research, which provides for the detection of epidemically current causative agents of acute respiratory diseases and their antigen and strain variants and for the study of their periodicity and dynamics of circulation during different seasons of the year in different territories, as well as for the establishment of their role in the genesis of acute respiratory diseases and pneumonias. A similar program also exists in the United States.

We have carried out a similar etiological supervision of acute respiratory diseases of noninfluenza etiology in the territory of our country and countries of the near abroad in the last 17 years. Constant monitoring of acute respiratory diseases is of great importance for the solution of practical and theoretical problems concerning the detection of patterns in the circulation of respiratory viruses in regions with different climatogeographical characteristics of territories and for the establishment of the natural variability of causative agents according to biological properties, as well as for problems of molecular epidemiology of respiratory virus infections.

Materials and Methods

Washes from the nasopharynx of people suffering from acute respiratory diseases served as material for the isolation of the virus. For the isolation of the virus a broad spectrum of tissue cultures both initially trypsinized and transplanted was used. The type to which viruses belonged was determined in the neutralization reaction with monospecific immune rabbit serums in a tissue culture. For virus identification electron microscopy and immunofluorescent and immunoenzyme methods were also used.

Results and Discussion

During the period from 1976 through 1993 more than 3,000 strains of viruses from nasopharyngeal washes from people suffering from acute respiratory diseases were isolated and identified. Adenoviruses of various serologic types were isolated most frequently in all the country's regions. Viruses of the Coxsackie B group, primarily of the third serologic type and the respiratory syncytial (RS) virus, were the next in significance.

The type landscape of adenoviruses circulating in the country's territory showed the primary spread of serotypes 2 and 3. A tendency toward an increase in the proportion in the population structure of adenovirus of type 4, as well as of latent serotypes 1 and 5, has begun to appear in the last few years. It should be noted that the frequency of isolation of the herpes simplex virus of type 1 has increased almost sevenfold in the last few years.

The spread of respiratory viruses in the country's different regions was not the same. For example, adenoviruses were more often isolated in Ukraine and the causative agent of RS-virus infection, in the Belarus Republic and in Russia (in its North-West Region and in the Far East). Picornaviruses were widespread in the Urals and in the Belarus Republic.

Epidemically current serotypes of adenoviruses (3, 4, 7, and 21) were more often isolated in Russia's North-West Region and latent ones, in the Belarus Republic and Ukraine. The epidemically current adenovirus of serotype 3 was dominant in all the country's regions.

On the basis of long-term observations we established a certain cyclicity in the spread of adenoviruses during different years of observation. For example, for the adenovirus of type 7 its maximum isolation occurs every 4th year, for the adenovirus of type 3, every sixth year, and for adenoviruses of types 1, 2, and 5, every 5th year of observation.

Table 1 presents data characterizing the change in current serotypes of adenoviruses—causative agents of acute respiratory diseases —in the country's population during different years of observation (1980-1992). It is evident that during the first 2 years the serologic type 3 was prevalent in the circulation among adenoviruses and the adenovirus of type 2, during the next 5 years. The adenovirus of type 5 held the first place in circulation only in 1985-1986. During subsequent years the adenovirus of type 3 again was prevalent in circulation. During the entire period of observations the adenovirus of type 1 held the third place after types 2 and 3. With regard to the adenovirus of type 7 it can be said that before 1988 it held one of the last positions in circulation, but since 1988 it has moved to the third place in significance.

Table 1. Change in Current Serotypes of Adenoviruses—Causative Agents of Acute Respiratory Diseases in the Country's Population During Different Years of Observation (1980-1992)

Years	Number of Identified Strains	Epidemically Current Types of Adenoviruses
1980-1981	253	3,6,1,7
1981-1982	244	3,2,1,6
1982-1983	268	2,3,1,6
1983-1984	643	2,6,1,4
1984-1985	253	2,6,1,3
1985-1986	110	5,3,6,7
1986-1987	183	2,3,4,5
1987-1988	348	2,3,1,5,7
1988-1989	330	3,2,7,1
1989-1990	207	2,1,7
1990-1991	250	3,2,4,1
1991-1992	253	3,2,1,4,5

According to the data of foreign authors [5-7], the adenovirus of type 7 was prevalent in the circulation in European countries and the serotype 2 of the adenovirus, in the east. Taking our long-term experience in the observation of the circulation of adenoviruses into consideration, it can be assumed that in our country the circulation of the most epidemiologically current serotypes of adenoviruses (types 3 and 7) corresponds to such in the territory of countries of the Far East (the eastern variant).

In the group of Coxsackie B viruses during the entire period of observation the serologic type 3 held the first position (Table 2) and the second and third place belonged to serotype 5.

Table 2. Change in Current Serotypes of Picornaviruses (Coxsackie B and Echo) Isolated From Patients With a Diagnosis of Acute Respiratory Diseases During Different Years of Observation (1980-1993)

	Epidemically Current Types During Indicated Years of Observation			
Causative Agent	1980-1983	1984-1986	1987-1989	1990-1993
Coxsackie B	3,5	3,5,6	3,2,5	3,4,1
Echo	11,12,19	6,1,9	6,19	1,8,19

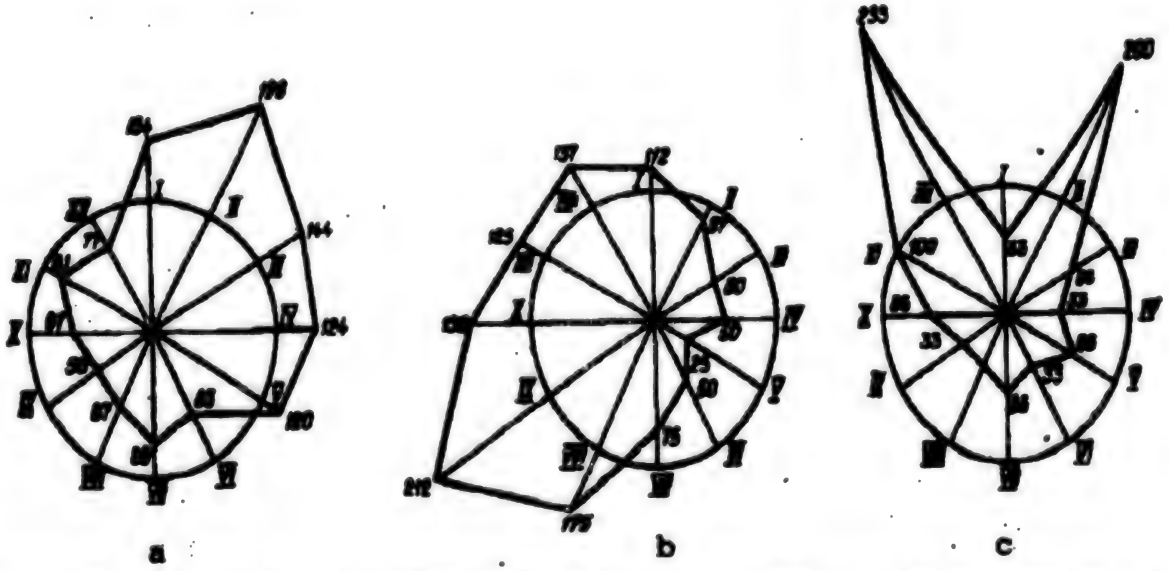
Table 3 presents data reflecting the change in current serotypes of adenoviruses in the country's population in different age groups and during different years of observation.

Table 3. Change in Current Serotypes of Adenoviruses—Causative Agents of Acute Respiratory Diseases—in the Country's Population in Various Age Groups During Different Years of Observation

	Epidemically Current Types During Indicated Years of Observation			
Age, Years	**1980-1983**	**1984-1986**	**1987-1989**	**1990-1993**
Up to 1	3,2,4,6,7,1	2,6,1,3,4	2,3,1,7,4	3,1,4,5,7
1-2	3,2,1,4,5,6	2,6,1,3,4	2,3,1,5	2,4,1,3
3-6	3,1,6	2,6,3,4,7	2,3,1,6(7)	2,4,1,3
7-16	3,1,5,6	2,1,6,3,4(5)	3,2,1,5(7)	2,3,1,4
17 and older	2,7,3,6	2,6,4,1,3(7)	2,3,7,5	3,2,1,7

From Table 3 it is evident that for children of younger and older age groups the epidemic type 3 of the adenovirus and the latent type 2 were of primary significance. In adults during the entire period of observations in the first place the adenovirus of type 2 was isolated primarily and epidemically current adenoviruses of serotypes 3 and 7 were second in significance. During the last years of observation (1990-1992) in children of younger age groups the adenovirus of type 4 hel . the second and third position in significance.

It is known that the seasonal nature of the spread of most respiratory viruses is their characteristic feature. In the course of research we detected seasonal fluctuations in the levels of the population's infection with these causative agents. A comparison of the isolability of respiratory viruses and of the herpes simplex virus of type 1 during different months disclosed significant fluctuations in the population's infection with these causative agents (see figure).



a b c

Seasonal Fluctuations in the Activity of Circulation of Adenoviruses of Serotypes 1-7, 21 (a), RS-Virus (b), and Herpes Simplex Virus of Type 1 (c)

Thus, the total infection of the country's population with adenoviruses of various serotypes was determined below the average annual level during a long period—from June through December. An excess of the average annual level of infection for the entire group of adenoviruses was noted from January through May with a

peak in February. For the RS-virus the level of infection exceeding the average annual level encompasses periods from August until January with a peak in September and for the herpes simplex virus of type 1, from November through February with a peak in December and January. Observing herpes infection for a long time, we noted that a rise in diseases of this infectious form precedes an influenza epidemic, or occurs simultaneously with it. As it seems to us, this is connected with a decline in the population's immunity as a result of a previous influenza infection and the activation of the herpes simplex virus of type 1.

The intensity of the epidemic process in acute respiratory diseases of picornavirus etiology increases with the onset of summer and greatly declines during other periods of the year.

Conclusions

1. Adenovirus infection in the territory of Russia and the near abroad was spread everywhere. The maximum level of circulation of adenoviruses was detected in Ukraine's territory. Epidemically current types of adenoviruses were established for the country's individual regions. The respiratory syncytial virus was more often isolated in Russia (North-West Region) and the Far East.

2. Epidemically current types of picornaviruses were determined for the country's entire territory with the maximum level of diseases in the Belarus Republic (Mogilev) and in Russia (the Urals and West Siberia).

3. A change in individual serologic types of adenoviruses and picornaviruses in the country's territory was shown.

4. It was established that in all age groups of people with a diagnosis of acute respiratory diseases adenoviruses of serologic types 1, 2, and 3 were prevalent in the frequency of isolation.

5. The peak of circulation of causative agents for the entire group of adenoviruses occurs in February, for respiratory syncytial virus infection, in September, and for herpes infection, in December. For picornaviruses of the Coxsackie B and Echo group the peak of diseases was noted during the summer period of the year.

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State and Characteristics of Development of Domestic Medical Instrument Making[1]

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[Article by Doctor of Technical Sciences V.A. Viktorov, corresponding member of the Russian Academy of Medical Sciences, director-general of the VNIIMP-VITA Joint-Stock Company]

[FBIS Translated Text] The international exhibitions "Public Health-93" (September 1993) and "Medical Equipment-94" (March 1994) held in Moscow were very representative. Many countries, including advanced ones in the field of medical instrument making, took part in them. Principal foreign and domestic firms, enterprises, and organizations of this specialization were their exhibitors.

The exhibition "Public Health-93" was the larger one. The total number of participating firms, enterprises, and organizations was more than 450, among which there were more than 240 from the Russian Federation. More than 230 exhibits, including about 130 from the RF, were presented at the "Medical Equipment-94" exhibition.

The wide participation of various domestic enterprises and organizations was an important feature of these exhibitions. This reflected the expansion of the circle of developers and manufacturers of medical equipment, which has taken place in our country recently, in particular, the appearance of new conversion-based defense enterprises.

Furthermore, quite many joint (foreign and domestic) firms displayed their products, especially at the "Medical Equipment-94" exhibition.

Forms of their joint activity are diverse. There are organizations that are only intermediate and their work is of a commercial nature. Some carry out the assembly of articles with the use of foreign units and elements. Others, at consumers' requests, complete sets and systems of instruments and apparatus, deliver and set them up, and provide the necessary services. With the help of these organizations a number of problems concerning the provision of medical institutions with modern medical instruments and apparatus are solved.

The generalization of data derived from the exhibitions and of special literature data on the development of domestic medical instrument making indicates that, recently, much fewer obsolete models have been manufactured and put into operation. Throughout the country in 1993 new articles with a run not exceeding 2 years made up about 35 percent in the total volume (according to the products list), up to 5 years, approximately 65 percent, and more than 5 years, only 35 percent, whereas in 1988 the share of articles with a run of less than 5 years made up 35 percent and more than 5 years, 75 percent. At the same time, even now there is a shortage of many simple and, accordingly, cheap articles.

Mostly articles in the fields of therapy (about 70 types) and of functional (about 65) and topical diagnosis (about 60) were shown at the exhibitions. Comparatively few laboratory diagnosis instruments were displayed, which reflects the insufficient level of their development in our country.

Among functional diagnosis equipment electrocardiographic equipment stands out in its significance. In Russia, despite the numerous developments in this direction, there are significant shortcomings in the output of the necessary equipment. Basically, single-channel electrocardiographs have been developed and are used in a comparatively wide manner, whereas in foreign practice their output does not exceed 10 percent of the total volume. They are manufactured by the Izhevskiy Motozavod [Izhevsk Motor Plant] Production Association. Instruments of the Lvov Radioelectronic Medical Equipment Plant are also widely operated. Basically, these electrocardiographs conform to modern requirements.

The Parus single-channel electrocardiograph developed by the Medkom Joint-Stock Company and by the Kometa Central Scientific Production Association (Moscow) has been developed recently and is in comparatively big demand. It possesses comparatively high indices: EKG analysis according to 12 leads and small weights (1.3 kg) and overall dimensions (228x136x50 mm). It is supplied with a liquid crystal screen. However, the instrument is outfitted with a printer (Elektronika MS-6312), which is not evaluated as sufficiently reliable.

In many cases 12-channel electrocardiographs of the EK 4MP-113051 type manufactured by the Yugmera Production Association (Krasnodar) are used. They are similar to the model manufactured in the past by the Hewlett-Packard firm (the United States). Cardioanalyzers of the TsN3052 type with syndromic diagnosis are also used widely. In a number of indices these models are greatly inferior to modern foreign analogs.

Systems and sets for automated EKG processing, including with syndromic diagnosis of about 20 models, were widely displayed at the exhibitions. They are still little used. Their comparative data and a sufficiently complete evaluation are as yet absent. Unfortunately, the simplest three-channel electrocardiographs meeting modern requirements, which are needed to widely outfit the country's medical organizations, were absent from the exhibitions and, according to available data, are not manufactured in our country. This is a significant shortcoming in domestic medical instrument making.

At the same time, the exhibition showed a significant expansion of our activity with regard to the development and manufacture of a number of functional diagnosis instruments.

For a long time instruments for the determination of respiratory functions were manufactured in our country mainly according to the developments of VNIIMP [All-Union Scientific Research Institute of Medical Instrument Making]. Ten systems for the determination of respiratory functions manufactured by the country's eight enterprises and organizations were displayed at the exhibitions under consideration. They include the computer speedometer by the VNIIMP-VITA Joint-Stock Company with an original design of the converter of air flow into a signal. A number of developments of the Tipaz Joint-Stock Company, in which measurements are not limited to the determination of forced discharge parameters alone, were shown. The instrumental part of these developments was executed on a high technical level.

The exposition of a number of new facilities based on the use of thermal viewing, radar, and radiometry, to which, in particular, the following pertain, deserves attention:

—radiothermographs and radiothermoscopes for the investigation of deep thermal fields of the human body and head, which represent highly sensitive radiometers with a set of antennas—applicators connected to computers and operating in the range of decimeter waves. The information issued by these radiothermographs and

radiothermoscopes has the appearance of temperature and color pictures (they have been developed and are manufactured by the Scientific Engineering Center of Biomedical Radio Electronics);

—an original system of dynamic thermal viewing with a high temperature sensitivity (00.1 °C), which makes it possible to uncover affected regions of human organs (it has been developed and is manufactured by the Institute of Radio Engineering and Electronics of the Russian Academy of Sciences (Moscow) and the OPTROS Limited Partnership (Novosibirsk);

—the Pulsar-004 radar instrument, which measures remotely (through dressing and clothing) the microshifts in the patient's integument and makes it possible to uncover blood flow and respiration indices (developer—the Moscow Power Engineering Institute).

The exposition of the Russian Academy of Sciences "Heart Rhythms," which showed a set of facilities for a quick evaluation of the patient's state according to his pulse, was of great interest. According to the results of measurement of pulse indices with the use of a computer device, a number of diagrams are plotted, gastrographic, autocorrelation, and spectral analyses are made, indices of cardiac activity and mental and psychophysical stability are determined, and Ryufer's [transliterated] test for the determination of man's fitness is realized. On the basis of these data generalizing conclusions are worked out.

The use in medical practice of pulsoximeters, which measure the degree of blood saturation with oxygen and the pulse, have acquired great significance recently. Their application has become obligatory during the control of patients' state in anesthesiology, intensive therapy, and reanimation.

In this field our country lagged behind advanced countries. By the beginning of 1993 the necessary instruments were developed and applied: The VNIIMP-VITA Joint-Stock Company developed the Oksipuls-01 instrument and then the Optim Scientific Production Firm (Nizhniy Novgorod), the Optim-420 instrument. Basically, these instruments correspond to foreign analogs in precision and functions, but are inferior to them in weights and overall dimensions. Six types of similar instruments, including the ELOKS-01M3 (Samara) with reduced weights and overall dimensions, as well as a portable instrument developed by the Bion Joint-Stock Company (Moscow), have already been displayed at the exhibitions.

Among topical diagnostic equipment (introscopy) roentgen and ultrasound instruments find wide application in medical practice.

Domestic organizations have shown much more roentgen equipment than during past years. However, the necessary development of digital roentgen has not yet been ensured in the country. In this connection the display at the "Medical Equipment-93" exhibition of the Diaskan roentgen scanning digital complex developed by the Special Design Office of Medical Roentgen Equipment (Moscow) jointly with the Medtekh Limited Partnership (Novosibirsk), which will be manufactured serially in the current year, deserves special attention.

Developments of new digital roentgen systems are also carried out by the Institute of Nuclear Physics imeni G.I. Budker (Novosibirsk) jointly with the Siberian Department of the Russian Academy of Sciences and by the State Scientific Research Institute of Aviation Systems jointly with the Moscow Oblast Clinical Scientific Research Institute imeni M.F. Vladimirskiy and the Ekran Scientific Production Association. The results obtained were displayed at the exhibitions. Problems concerning the organization of the series production of these systems have not yet been solved.

In the area of development of domestic roentgen equipment important work has been done on improving apparatus of the RUM-20 type, which are serially manufactured by the Mosrentgen Joint-Stock Company, as well as on developing similar new ones. The RUM20M-SG312 roentgen complex, which can be delivered with domestic intensification of the brightness of the roentgen image of the Sapfir type, or with French-produced intensification of the brightness of the roentgen image, was shown. The Moscow Special Design Office of Medical Roengten Equipment displayed the RDK 50/5 photographic roentgen diagnostic complex in G 202-5 modification, which represents a universal apparatus for scanning and layer photography of the patient in a lying position. This apparatus is supplied with a feeder (PURS), which makes it possible to photograph in manual and automated regimes with automatic organ equipment according to the laying atlas. It is equipped with a microprocessor control system, which promotes a high stability of photograph parameters.

The Elektron Scientific Research Production Complex (St. Petersburg) showed the new mobile RST-61 roentgen television unit for surgery, orthopedics, and traumatology, which is of considerable interest.

The activity in the area of development of medical diagnostic nuclear magnetic resonance systems is noted for complexity and labor intensiveness. A marked lag behind advanced world countries was observed in this sphere in our country until recently. Fortunately, the situation is changing now.

The following new domestic diagnostic nuclear magnetic resonance systems were displayed at the exhibitions: Obraz-3 and ICONA-6400 delivered by MOZ Agregat and Toros manufactured by the Servisinstrument Joint-Stock Company. Basically, these systems meet modern requirements.

In the last two decades advanced world countries have paid especially much attention to the development of ultrasound diagnostic equipment, which also continues today. We also have achievements in the development of doppler instruments by the forces of the VNIIMP-VITA Joint-Stock Company on the basis of cooperation with foreign firms.

With respect to the display of domestic echotomoscopes a number of instruments developed in the RF and other CIS countries were shown. These are eight models of the simplest single-type instruments, mainly, with mechanical sector scanning, and several instruments with electric linear scanning, small sets of sensors, and very limited functional capabilities. In this field we greatly lag behind advanced foreign firms.

In the exposition of Russian endoscopic equipment, basically, flexible endoscopes developed and manufactured by the Leningrad Optico-Mechanical Association were shown. In a number of indicators they are close to foreign analogs, but are greatly inferior to them in reliability. The achievements of foreign firms in the output of endoscopes with a reduced diameter of their working part and in the application of television systems for the representation of images have not yet been realized.

Television systems for the representation of endoscopic images developed at the Zenik Scientific Production Complex, at the Elektron Scientific Production Complex (St. Petersburg), and at the VNIIMP-VITA Joint Stock Company should be included among the positive results of the development of domestic endoscopic equipment achieved most recently.

The level of development of medical laboratory equipment in our country does not meet the country's needs in terms of the list of products, their production volumes, and, to a large extent, the technical perfection of manufactured products. Only some of the latest meet modern requirements to a sufficient degree, in particular, radioimmunological instruments developed by the VNIIMP-VITA Joint-Stock Company, which are not inferior in their technical level to the best foreign analogs.

The exhibitions showed that a tendency toward an improvement in the state of affairs in this field has appeared in the last few years. Whereas previously the development of the necessary instruments, basically, was ensured by the All-Union Scientific Research and Design Institute of Medical Laboratory Equipment (St. Petersburg), now instruments are developed by the forces of nine developer organizations. Among them three are comparatively large: The Proba Scientific Production Enterprise (St. Petersburg), the Scientific Research Institute of Biological Instrument Making (Moscow), and Tekhnomedika (Moscow). For now, however, these developers and manufacturers create comparatively simple instruments with limited functional capabilities.

A comparison of domestic and foreign products of diagnostic laboratory equipment shows that many necessary instruments are not manufactured at all, or are greatly inferior to foreign ones. In particular, they include automated integrated analyzers, as well as most instruments for routine work, including electronic laboratory precision scales, equipment for dosing liquids, pH-meters, and elements of the technology for the manufacture of products from various polymeric materials.

A comparatively large amount of therapy equipment was shown at the exhibitions by many domestic enterprises and organizations. It included laser technology products and magneto-therapy, electric stimulation, ultrasound, irradiation, and galvanization apparatus.

The development of therapeutic laser apparatus in our country is carried out rapidly and on a comparatively high level. Domestic laser apparatus possess higher indices and are noted for a lower cost than foreign ones.

About 30 types of domestic laser apparatus for medical purposes were shown at the exhibition. Most of the exhibited apparatus are of the same type. This is connected with the fact that, recently, many defense industry enterprises have begun to develop and produce medical laser instruments by way of conversion and in a number of cases this is done without a sufficiently advanced substantiation of the advisability of selected technical solutions, by analogy.

At the same time, some organizations conduct efficient research in this field and develop original products. In particular, the results of activity of the MAKDEL Association (Moscow) are very interesting. It unites laserologist researchers, practitioners, and developers and manufacturers of apparatus. The association has shown a number of new laser apparatus, in particular, for the treatment of internal organs and purulent wounds and for reflex therapy, as well as for ophthalmological purposes—for the treatment of dystrophy of the optic nerve, functional myopia, and so forth.

An overall utilization of laser apparatus jointly with other therapeutic effect facilities is one of the important tendencies in the development of domestic medical

therapeutic equipment. In particular, the development of the following should be noted:

—a laser computer cabinet equipped with a helium-neon laser, a semiconductor magnetic laser, a portable widely functional semiconductor laser, and the Limb electrolaser puncture instrument for application in various fields of medicine and realization of a wide range of therapeutic effects (developer—the Dalmedservis Scientific Production Center, Vladivostok);

—the MILTA magneto-infrared laser therapeutic apparatus for the treatment of internal organs, wounds, ulcers, bone injuries, arthritides, ischemic heart disease, and so forth [the State Production-Design Enterprise for Humanitarian Information Technologies (PKP GIT), Moscow];

—the Lazur magnetolaser apparatus, which contains 20 laser emitters for radiotherapy for throat cancer (the Magnetron Scientific Production Complex, Kaluga).

Low- and high-frequency apparatus developed basically by the All-Union Scientific Research Institute of Medical Instrument Making, including low-frequency types Polyus-1, -2, -3, and -101 and high-frequency types Ultratron, UVCh [Ultra-High-Frequency]-30-2, decimeter wave-therapy Volna-2M, and centimeter wave-therapy Luch-11, have been widely used in the field of magnetotherapy for a long time.

Apparatus operating over extremely high-frequency ranges have been recently developed and are being used successfully. Treatment is carried out by a local effect on receptor fields or reflexogenic zones with low-intensity electromagnetic radiation. This occurs owing to the mobilization of reserve capabilities of the organism and increase in its immune status. Apparatus are used for the treatment of gastric and duodenal ulcers, cardiovascular diseases, vascular brain diseases, and dermatological, urological, and gynecological diseases. These types of products were displayed at the exhibitions: the Yav-1 apparatus developed by the Istok State Scientific Production Enterprise and the Istok-Sistema Scientific Production Enterprise (Fryazino, Moscow Oblast) and the Bayur-01 apparatus developed by the Scientific Research Institute of Measuring Systems and the Ring Small State Enterprise (Nizhniy Novgorod).

Among the new domestic facilities in the field of magnetotherapy shown at the exhibitions the following are of considerable interest:

—Magnitoturbotron-2 for the treatment of oncological patients [the essence of the realized method lies in a simultaneous effect on all human systems and organs of a rotational magnetic field with a cyclical change in its induction (developed by the Agregatnyy Zavod Scientific Production Complex and the Korporatsiya AGREGAT Joint-Stock Company)];

—a magnetotherapeutic correlation complex noted for an individual formation of an acting pulsed magnetic field with due regard for the patient's data [is used for the treatment of ischemic heart disease, gastric ulcer, complex fractures, and cerebral insults (is manufactured by the Alesya LTD Firm (city of Raduzhnyy)];

—light and inexpensive portable apparatus, Magniter, designed for the treatment of many diseases, including cardiovascular, radiculites, diseases of the support-motor system, prostate, and burns [developed by the Scientific Research Institute of Radio Communication (Nizhniy Novgorod)].

Activity connected with the development and output of electrostimulation equipment with the participation of many organizations and enterprises has greatly expanded in our country in the last few years. In particular, developments are carried out actively and the production of electrocardiostimulators, mainly implanted, has been organized. Ten types of apparatus are being manufactured and electrostimulators for the treatment of vascular and urological diseases are being produced.

A number of electrostimulation apparatus have been developed in our country on the basis of research conducted jointly by instrument making and medical organizations. Among those shown at the exhibitions the following pertain to them:

—the ELIMAN-401 bioregulated antipain electrostimulator based on the transcutaneous electrostimulation of nerve trunks. It is used for the relief of postoperative and traumatic pains during chronic pain syndromes and labor (development of Samara State Aerospace University imeni S.P. Korolev; Scientific Research Laboratory-43, Samara);

—the Mioton-604 six-channel programmed bioelectrical stimulator for the treatment of motor disorders, which can be used for direct control of the recipient's movement from the donor (is produced by the Arzamas Instrument Making Plant);

—the ophthalmological electrostimulator ESOF-1 developed by the Medsistem Joint-Stock Company (the Ekran-Market Firm, Moscow) for a therapeutic effect in myopia, hyperopia, and astigmatism;

—respiratory electrostimulators of ESD-2P and ESD-2N-N4 types designed for the treatment of acute and chronic respiratory insufficiency (developed in the Department of Medical Equipment of AGAT [expansion

unknown] of the Scientific Research Institute of Epidemiology and Microbiology imeni Louis Pasteur, city of Istra-2, Moscow Oblast).

As the exhibitions showed, in Russia ultrasound therapy equipment, irradiators, and illuminators, in particular those developed by the VNIIMP-VITA Joint-Stock Company, are manufactured on a modern technical level.

Domestic equipment for artificial lung ventilation and inhalation anesthesia were widely displayed at the exhibitions. Nine models for artificial lung ventilation were shown, six of which were developed by the VNIIMP-VITA Joint-Stock Company, including Spiron-201 for adults, high-frequency Spiron-601, Spiron-412 for children, Spiron-305 for anesthesia, manual ADR-1000 for adults, manual ADR-125 for children, and four apparatus for inhalation and intravenous anesthesia. These apparatus are evaluated as meeting modern requirements and in their functional capabilities conforming to foreign analogs.

The problem of the development of a domestic modern artificial blood circulation apparatus was solved in our country. The AIK-6.07 apparatus developed by the VNIIMP-VITA Joint-Stock Company displayed at the exhibitions is evaluated as conforming to the world technical level.

Problems concerning the development of domestic apparatus for artificial blood purification on the basis of the developments of the VNIIMP-VITA Joint-Stock Company, in particular perfusion units BP-03 and -05 and Renart-10 and -10RT apparatus, which were shown at the exhibitions, were solved on the same technical level. The application of a universal perfusion unit used not only for perfusion, but also for dialysis and ultrafiltration, is the distinctive feature of these apparatus. In their functional parameters and technical characteristics they conform to the foreign analog in this apparatus category.

Furthermore, the development of a detoxication apparatus carried out by the Kursk Pribor Production Association with the participation of the Fresenius Firm (Germany) should be considered an achievement in this area. The apparatus is noted for mobility and a small weight and small overall dimensions.

The exhibitions also displayed a number of domestic medical instruments and apparatus, which are of interest and deserve a highly positive evaluation. They reflected in a comparatively complete manner the state, development, achievements, and shortcomings of domestic medical instrument making and made it possible to obtain important information for an efficient utilization of the opportunities existing in the country and for the solution of problems concerning the further development of domestic medical equipment.

Footnotes

1. According to the data of the exhibitions "Public Health-93" and "Medical Equipment-94".

Status and Prospects of Creating New Synthetic Pharmaceuticals

957A0843A Moscow VESTNIK ROSSIYSKOY AKADEMII MEDITSINSKIKH NAUK in Russian Nov 94 No 11, pp 31-35

[Article by R. G. Glushkov, Center for Pharmaceutical Chemistry of the All-Russian Chemical Pharmaceutical Scientific Research Institute, Moscow; UDC 615.2/.3.038.07]

[FBIS Translated Text] Certain successes were attained in recent years in creation of new pharmaceuticals and in medicinal treatment of many diseases. However, this remains one of the most urgent problems of public health, side by side with urgently needed measures to provide effective pharmaceuticals to the public.

The need for creating new pharmaceuticals and replenishing the assortment of medications with modern preparations is brought about by the following circumstances: 1) a number of serious diseases still do not respond to radical treatment by currently existing preparations; 2) lengthy use of pharmaceuticals in therapeutic practice generates tolerant pathologies requiring new generations of medicinal agents, as a rule with a different mechanism of action; 3) new serious diseases for the treatment of which there are no effective preparations arise as a result of evolution of microorganisms; 4) undesirable side effects of medicinal agents are revealed in a number of cases, making it necessary to replace them by safer ones.

Naturally when the discussion turns to creating new pharmaceuticals, we have in mind fundamentally new medicinal agents with new mechanism of action, with their own therapeutic "niche," opening up new possibilities in the treatment of various diseases, and preparations which should supplant obsolete medications of greater toxicity in view of their higher effectiveness and safety. In this connection it is very important as early as in the preclinical research stage, and especially during clinical study of new pharmaceuticals, to have an effectively operating system for objectively evaluating their effectiveness and safety—a system that would allow medical use of only those preparations that are truly needed by public health and satisfy world requirements.

Examining the basic factors determining the directions of the search for new pharmaceuticals, we should emphasize that in recent years both the disease structure and the epidemiological situation changed significantly in the world community. In particular, noticeable aging of the population and a resulting increase in morbidity of elderly people are observed in a number of countries, and especially in highly developed states, in connection with the increasing average life span. These diseases include various forms of psychoneurological (dementia, parkinsonism, depression, sleep disorders) and cardiovascular diseases (atherosclerosis, impaired cerebral circulation, arterial hypertension, disturbed cardiac rhythm, cardiac ischemia etc.), diseases of the bearing-locomotor apparatus (arthritis, deforming and degenerative diseases of the vertebral column etc.), and lung diseases (bronchial asthma, chronic obstructive bronchitis, etc.).

This far from complete list shows how complex and multifaceted the problem of finding and creating new pharmaceuticals needed by public health is. An example might be development of preparations with which to treat senile dementia, particularly Alzheimer's disease, parkinsonism, and various depressed states. Special attention is now being devoted to preparations of this group because they can significantly influence the "quality" of life and considerably lengthen a patient's active life.

According to published data the main approach to creating geriatric preparations is that of seeking gently-acting medicinal agents that do not cause abrupt changes in basic body functions, and have therapeutic action due to their influence upon metabolic links of the pathogenesis of disease. In this connection many publications and patents have recently appeared, devoted to development of pharmacologically active substances influencing metabolism of amino acid neuromediators as well as new antioxidants and antihypoxicants, immunomodulators, and gently acting reversible inhibitors of cholinesterase and other enzymes.

Examining the paths of creation of new synthetic pharmaceuticals, I would like to emphasize that in recent years, in addition to traditional studies associated with screening biologically active compounds, which are still necessary today, research on directed synthesis of new preparations is playing an ever-greater role. This work includes studying the mechanisms of action, the pharmacokinetics and metabolism of drugs, including the drug-receptor system; revealing the role of endogenous compounds in biochemical processes determining a particular form of physiological activity; research on the possible ways of activating or inhibiting the body's enzyme systems; modifying molecules of known pharmaceuticals and endogenous compounds with regard for their structural features, particularly "pharmacophoric" groups, which contribute to establishment of their biological activity; enhancing the selectivity and biological accessibility and regulating the time of action of drugs by creating "transport" systems for pharmaceuticals as well as endogenous biologically active compounds, and development of pro drugs; revealing the correlation between structural factors, physicochemical properties and the biological activity of compounds, using computers to design drugs.

To illustrate this sort of research, we can cite in particular the work of our institute aimed at creating a preparation serving as a transport system for gamma-aminobutyric acid (GABA), which is the main mediator participating in central inhibition processes. We know that GABA has difficulty penetrating the hematoencephalic barrier, as a consequence of which certain difficulties arise in the treatment of neurological diseases, associated with regulating the GABA concentration in the brain necessary for a therapeutic effect.

As a result of research carried out in the Center for Pharmaceutical Chemistry (TsKhLS) of the VNIKhFI [All-Russian Scientific Research Chemical Pharmacological Institute], an original transport system was developed for biologically active compounds containing an amino group in their structure, including for GABA:

Key: 1—etc.

It should be emphasized that fragment A in compound I is not an acyl residue, but it is covalently bonded with the NH group. Connection of the NH group of GABA to the transport system by a covalent bond made it possible to obtain a preparation with new properties—rather high lipophilic properties and the ability to penetrate the hematoencephalic barrier rather easily—and one protecting the amino group of GABA from the inactivating action of enzymes such as aminoxidase.

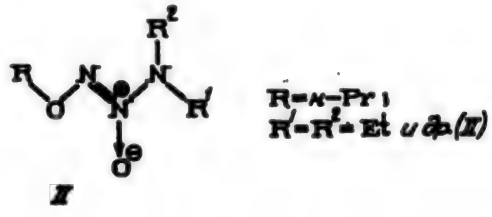
The main peculiarity of transport system I is its ability to split in the brain to release GABA; in this case the rate of release of GABA may be regulated by appropriate selection of the transport fragment A.

The TsKhLS VNIKhFI has for practical purposes completed preclinical study of the first representative of this

group of preparations, as a result of which the possibility of regulating the GABA concentration in the brain by means of type I transport systems was experimentally confirmed.

Another example of a promising direction in the search for new medications is creation of preparations that generate nitric oxide, which has a vasodilatory and antihypertensive action. Included among such substances are sodium nitroprusside (Nipride), as well as nitroglycerine and other nitrates which can generate nitric oxide as a result of biotransformation in the body. The mechanism of action of nitric oxide is associated with its ability to activate soluble guanylate cyclase, which raises the concentration of cyclic guanosine-3',5'-monophosphate, and ultimately increases vasodilation. It should be emphasized that the existence of endogenous nitric oxide, formed due to oxidation of an amino acid—l-arginine—was also demonstrated.

Recently published data on new compounds—oxotriazene derivatives (II) which are pro drugs in relation to nitric oxide—may be cited as an example of promising preparations currently under development as nitric oxide generators, having an antihypertensive and vasodilatory action:



Some of these compounds display antihypertensive activity higher than that of sodium nitroprusside and longer action in experiments on animals [3]. However, use of II compounds as the basis for creating new antihypertensive drugs may encounter certain difficulties in my opinion, associated with their insufficient stability, high toxicity, and other undesirable properties inherent to nitric oxide derivatives.

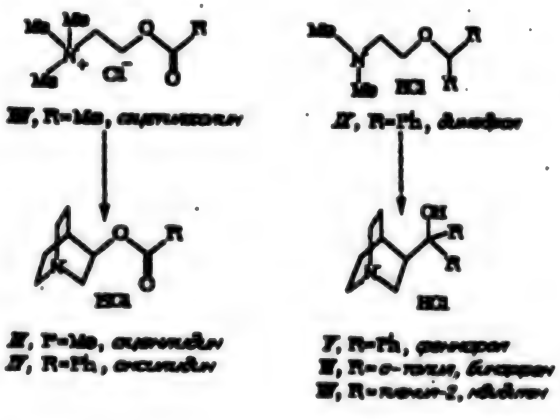
In this connection it would seem suitable to search for antihypertensive preparations among nitrogen-containing compounds which, as with l-arginine, do not have the elements of nitric oxide in their structure but which may generate it in the course of biotransformation in the living organism.

Looking at research directed specifically at finding new synthetic preparations, I would like to emphasize that one of the most widely used methods of designing drugs today is modifying the structure of known preparations associated with the most important mediators of biochemical processes. The success that has been achieved in this area can be illustrated with specific examples from creation of original preparations in the TsKhLS VNIKhFI. Included among them is the discovery, development and introduction of the following three classes of pharmaceuticals into medical practice: 1) original preparations of the quinuclidine series; 2) tetracyclic antidepressants of the pyrazinocarbazole and pyrazino-β-carboline group; 3) anticancer preparations—derivatives of dyspyrotripiperazine.

Mention should be made of the enormous amount of work done by the TsKhLS VNIKhFI with the participation of many scientific and clinical institutions to create the original preparation Arbidol, which has immunomodulating and interferon inducing properties, and which has been passed for medical use as a drug to prevent and treat types A and B influenza and other acute respiratory viral infections [1].

Presence of antioxidant properties is an important feature of Arbidol as a preparation with a wide spectrum of biological activity. These properties provide the grounds for anticipating use of this compound also against pathologies associated with an elevated concentration of peroxide compounds and free radicals in the body.

The procedure by which the following original preparations are created at the TsKhLS VNIKhFI in the quinuclidine derivative group is diagrammed below: The cholinomimetic aceclidine (III); the tranquilizing and hypotensive drug oxylidine (IV); the antihistamine and antiallergic drugs Fenkarol (V) and Bikarfen (VI) [transliterations] [2]; and the anti-ulcer preparation Kviditen (VII), which is now undergoing the second phase of clinical study:



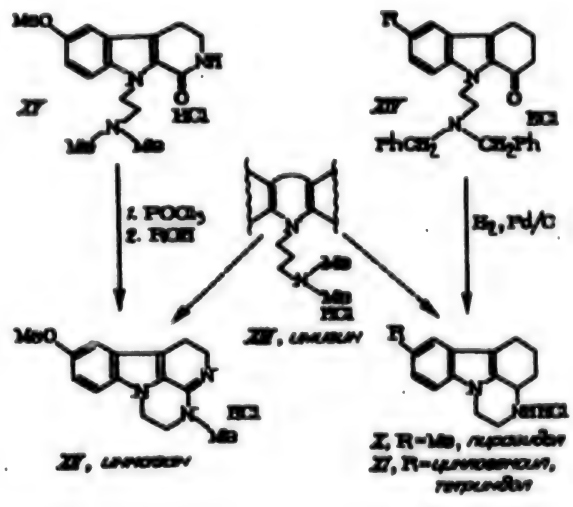
Creation of these preparations is based on the general principle of modifying molecules of the neuromediator acetylcholine (VIII) and the antihistamine preparation Dimedrol (IX) [2] by connecting their pharmacophoric fragments (N,N-dialkylaminoalkyl residues) into a conformationally rigid quinuclidine structure with a shielded free pair of electrons on the nitrogen atom. Transition to a quinuclidine structure in preparations III-VII makes it possible to fix the mutual positions of structural elements and functional groups in their molecules that are responsible for interaction with the corresponding receptor systems of the body.

When acetylcholine (VIII) was used as the prototype compound, the transition to aceclidine (III) turned out to be rather simple, and acquisition of a new type of biological activity simply required inclusion of the aminoalkyl pharmacophore of acetylcholine in the cyclic system of quinuclidine with a tertiary nitrogen atom. Modification using the III acyl fragment made it possible to obtain oxylidine (IV). During design of the antihistamine preparation Fenkarol (V) using IX as the model compound, it was discovered that simple inclusion of the aminoalkyl pharmacophore into the quinuclidine system is insufficient, and that the diphenyloxymethine pharmacophore had to be modified. Such modification made it possible to obtain a preparation with qualitatively new properties. Thus like Dimedrol (IX), Fenkarol (V) is an H^1-histamine receptor blocker, but in contrast to IX its lipophily is lower. In this connection V penetrates poorly through the hematoencephalic barrier, and it does not have an undesirable sedative and soporific side effect. In addition V activates the diaminoxidase fragment, which in turn inactivates histamine in the tissues, which intensifies the antihistamine activity of Fenkarol to a significant degree.

Further modification of the structure of Fenkarol by substitution of phenyl radicals by orthotolyl fragments made it possible to obtain the preparation Bikarfen (VI), which in contrast to Fenkarol has antiserotonin activity, and in this connection manifests higher effectiveness against allergic and other diseases accompanied by dermal pruritus.

When 2-thienyl residues were included in the structure of Fenkarol in the place of phenyl radicals, the anti-ulcer preparation Kviditen (VII) was obtained, which is in the M^1-cholinoreceptor blocker group. Experimental and clinical data show that VII is superior in its effectiveness to the known preparation Pirenzepine (Gastrozepin), and in addition it possesses gastroprotective properties in the presence of erosive injuries to the gastric mucosa, the esophagus and the duodenum.

The procedure for creating original tetracyclic antidepressants—Pyrazidol (X), Tetrindol (XI) and Incazan (XII)—is presented below [2]. The structure of these preparations was once again based on the general principle of modifying molecules of the known tricyclic antidepressant Imizin (Melipramin) (VIII) [2]. The starting compounds in this case were structural analogues of Imizin—derivatives of carbazole (XIV) and β-carboline (XV), the aminoalkyl fragments of which were included in the piperazine ring, resulting in the formation of previously unknown tetracyclic systems.



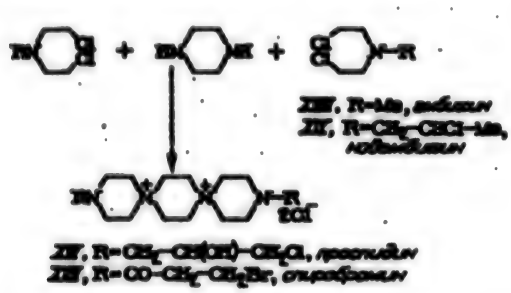
It should be noted that the transition from model compounds XIV and XV (structural analogues of XIII) to tetracyclic preparations X-XII was accomplished by single-stage methods. Thus, X and XI were obtained by hydrogenating the corresponding compounds XIV over Pd/C, while XII was synthesized by cyclizing XV with phosphorus oxychloride followed by decomposition of the intermediate complex by boiling in alcohol.

The three original antidepressants obtained in this way (X-XII) are classified by their mechanism of action in the group of selective and reversible monoaminoxidase A inhibitors, and they differ from tricyclic type XIII antidepressants or amitriptyline in having no cholinolytic side effects.

It should be emphasized that Pyrazidol, Tetrindol and Incazan exhibit certain differences both in the expressiveness of antimonoaminoxidase activity and other biochemical effects (influence on reverse neuron capture and on binding with receptors), and in the strength and spectrum of psychopharmacological activity, in connec-

tion with which each of these preparations has its own therapeutic niche.

The procedure for creating the original antitumor preparations Prospidin (XVI) and Spirobromin (XVII) [transliterations], developed in the TsKhLS VNIKhFI and placed in the dyspyrotripiperazine group is presented below:



Known antitumor drugs with alkylating action—Embichin (XVIII) and Novembichin (XIX), for which bis-(β-chlorethyl)-amine groups are the principal pharmacophores—may be viewed as the prototype compounds for development of the structure of XVI and XVII. Inclusion of these groups in the cyclic dyspyrotripiperazine system together with connection of additional alkylating substituents to the terminal (tertiary) nitrogen atoms of this system made it possible to obtain preparations XVI and XVII with new pharmacotherapeutic properties.

The main indications for use of Prospidin are laryngeal cancer and malignant pharyngeal neoplasms. In contrast to other cytostatic drugs, at therapeutic doses Prospidin does not have pronounced inhibitory action upon hemopoiesis [1].

Spirobromin is used in combined chemotherapy of acute leukosis as well as against malignant lymphomas, laryngeal cancer, dermal reticulosis and some other oncological diseases [1].

Summarizing the material presented here, I would like to emphasize that a general principle that may be formulated as follows was laid at the basis of creation of all of these three classes of original pharmaceuticals with different spectra of biological activity: Modification of the structure of biologically active substances by complete or partial inclusion of their "pharmacophoric" groups in cyclic systems makes possible a transition to compounds with qualitatively new biological activity.

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Synthesis and Immunotropic Activity of Benzopyrane-2-one Derivatives

957A0837A Moscow
KHIMIKO-FARMATSEVTICHESKIY ZHURNAL
in Russian Nov 94 Vol 28 No 11, (manuscript received 23 Sep 93) pp 20-22

[Article by A. Z. Abyshev, G. I. Nezhinskaya and K. Ch. Melikov, Vaccines and Sera Institute, St. Petersburg; UDC 678.447.42- 134.26.615.717]

[FBIS Abstract] The results of investigations of some copolymers in the benzopyrane series (CP-I-V), obtained for the first time by the authors, are presented. These macromolecules are shown to exhibit different immunotropic activity with respect to the composition of comonomers, structure, molecular weight, hydrophilic and hydrophobic properties. It is clear that CP-I and CP-V may be classified as thymus-nondependent antigens with respect to the degree of their impact on murine immune responses. The higher hydrophilic capacity of the CP-V molecule has an effect on B lymphocytes, resulting in a reduction in the murine splenic count of antibody-forming cells. The inclusion of imidazole, benzimidazole and other heterocycles into the polymer chain makes CP-II and CP-III close to thymus-dependent antigens, as is manifested by elevated murine splenic levels of E-rosette-forming cells (this requires further confirmation). Inclusion of a maleimide fragment gives rise to conjugated compounds with various antigens. Immunization of rabbits with the conjugates yields antibodies with a titer 1:25,000+/-521. The findings indicate that all the tested compounds have features in common, specifically, they have an intensifying effect on humoral immune responses, the presence of T lymphocytes with histamine receptors, enhanced T-suppressor activity of lymphocytes and the appearance of sufficient quantities of immature forms of macrophages. These data confirm the involvement of many immunity structures in response to administration of the studied copolymers. The conjugation of the studied immunomodulators with antigens of various viruses will make it possible to obtain highly active antibodies needed in developing combined preparations for treating and preventing viral infections. Figures 2; references 18: 16 Russian, 2 Western.

Frontal Polygons Method: New Approach to Analysis of Structure—Biologic Activity Interrelationship

957A0837B Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Nov 94 Vol 28 No 11, (manuscript received 5 Aug 93) pp 32-35

[Article by A. I. Khlebnikov, Altay Technical University imeni I. I. Polzunov, Barnaul; UDC 577.3+547.9+615.015]

[FBIS Abstract] A new method has been developed which makes it possible to find the common structural elements in series of compounds of different classes and which also takes into account both the geometric similarity of the studied chemicals and the properties of their atoms. The proposed approach differs advantageously in many ways from the system in current use in Russia and that described by A. K. Ghose, et al. in J. COMP. CHEM., Vol 6, No 5, pp 350-359, 1985. The deficiencies in these systems are pointed out and the advantages afforded by the new approach are outlined. The new method is based on the identification of relatively planar peripheral sites in the molecule and on their comparison with the similar sites of other molecules. The structure of the pertinent algorithm is discussed. A biological activity-structural relationship can be established within the framework of the proposed approach. Specific detailed examples are given of search for the common structural moieties for nonnarcotic analgesics: para- acetaminophenol, acetylsalicylic acid and amidopyrine. It cannot be said that development work along these lines has been completed; work is continuing for raising the method to a quantitative level and on its application to different series of biologically active substances. References 11: 8 Russian, 3 Western.

Influence of Lipid Concentrate From Aboveground Part of Ajuga turkestanica on Metabolic Processes and Dynamics of Experimental Skin Wound Healing

957A0837C Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Nov 94 Vol 28 No 11, (manuscript received 19 Nov 93) pp 46-48

[Article by V. N. Syrov, Z. A. Khushbaktova, I. Tolibayev, N. V. Yeletskaya and A. U. Mamatkhanov, Chemistry of Plant Substances Institute, Uzbek Academy of Sciences, Tashkent; UDC 615.322:582.949.22].015.4.07]

[FBIS Abstract] Neutral lipids were extracted from the dried and pulverized aboveground part of Ajuga turkestanica (Rgl.) Brig, collected in the flowering stage, by extraction with chloroform while steeping at room temperature. The experiments were conducted with male rats weighing 150-180 g. The lipid extract was applied to the shorn skin on the back once each day. The efficacy of the preparation on metabolic indices of the skin was evaluated 15 and 30 days after onset of the experiment. After the animals were sacrificed the treated skin was subjected to biochemical study. The study revealed that the use of a lipid concentrate derived from the aboveground part of this plant as applications in 0.5 percent cotton oil concentrates results in the activation of skin metabolic processes after 15-30 days. There is an elevation of its total protein and glycogen, an increase in the redox potential of the lactic-pyruvic acid system, a reduction in the ratio of cholesterol to phospholipids and potassium to sodium. A slight hydration occurs in the tissue. A morphologic examination revealed a more marked formation of skin appendages in comparison with the control. A noticeable increase in their number is observed in the microscopic field of view, young hairy follicles being predominant. The healing of cleansed skin wounds is accelerated by the lipid concentrate from this part of the plant. It may be a useful biocomponent in producing various cosmetics and perfumeries for prevention and treatment of skin ageing and as a wound-healing agent. Figure 1; references 23: 15 Russian, 8 Western.

Cloning and Expression of Gene of Phosphatidylinositol-Specific Phospholipase C From Listeria Monocytogenes Cells

957A0750A Moscow MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 6, Nov-Dec 94 (manuscript received 29 Mar 94) pp 3-8

[Article by S. A. Yermolayeva, Yu. F. Belyy, I. S. Tartakovskiy, A. L. Gintsburg and S. V. Prozorovskiy, Epidemiology and Microbiology Scientific Research Institute imeni N. F. Gamaleya, Russian Academy of Medical Sciences; UDC 579.869.1:579.25].08]

[FBIS Abstract] The gene for phosphatidylinositol-specific phospholipase C (PI-PLC) from Listeria monocytogenes was cloned and the possibility of its expression in Eshcherichia coli both from its own, as well as from the lactose promoter was examined. The recombinant plasmid was constructed on the basis of the pR1T2T vector; it carries a hybrid gene, whose 5' end is a fragment of the protein A gene of Staphylococcus aureus. The 3' end is a gene for phospholipase plcA. Both are in the same reading frame. The resultant construction in Escherichia coli performs coding of the hybrid recombinant protein A:IPI-PLC. A purified preparation of the hybrid protein AIIPI-PLC and polyclonal rabbit

antiserum for it were obtained. The resulting antiserum for the hybrid protein, containing phospholipase as the C-end domain, is shown specifically to detect phospholipase both in the recombinant strain of Escherichia coli carrying the plasmid containing the gene of phospholipase under the control of the lactose promoter, as well as in the Listeria culture fluid. Figures 7; references 16: 2 Russian, 14 Western.

Construction of High-Level Expression Plasmid Vector for in vivo Delivery of Recombinant Biologically Active Proteins. 1. Synthesis of Antigenic Determinants of HIV-1 Proteins gp120 and gp41 in Enterobacteria

957A0750B Moscow MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 6, Nov-Dec 94 (manuscript received 1 Aug 94) pp 12-16

[Article by V. A. Belyavskaya, A. I. Zakabunin, I. N. Dolgova, S. I. Belikov, K. N. Verevkina and I. I. Krasnoborov, Scientific Research Design-Technological Institute for Biologically Active Substances, Berdsk; UDC 579.842.1/2:579.252.5]:279.25]

[FBIS Abstract] The plasmid vector pAZ was constructed specially for in vivo delivery of recombinant biologically active proteins, in particular, antigenic determinants. This vector meets the requirements on construction of recombinant bacteria as live per os carriers. The pAZ vector has a strong constitutive promoter, has high stability in cells of E. coli and the vaccine strain of S. choleraesuis, and also additionally encodes synthesis of the marker protein (β- galactosidase), which will later help in tracing the path of the bacterial vector in the macroorganism. Several recombinant plasmids encoding synthesis of β-galactosidase variants with insertions of short fragments of the HIV-1 gp41 and gp120 proteins, which were previously shown to be antigenic determinants, were constructed on the basis of the pAZ vector. Laboratory strains of E. coli and the vaccine strain S. choleraesuis were transformed by the recombinant plasmids. The level of synthesis of the hybrid proteins was dependent to a high degree on the inserted fragment. The maximum synthesis level in E. coli was 16 percent. The hybrid protein was isolated and purified (up to 90 percent) with a yield of 4 to 6 mg/g of wet biomass. Almost all the hybrid proteins were immunologically reactive, as shown by the immunoenzymatic method using both nonfractionated lysates and purified proteins. In both strains in vitro stability of the vector and recombinant plasmids was high and not less than 90 percent after 10 passages (about 140 generations) under nonselective conditions. Figures 2; references 26: 5 Russian, 21 Western.

Studies of Rickettsia prowazekii Antigens in Immunoblotting With Specific Sera of Infected White Mice

957A0750C Moscow MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 6, Nov-Dec 94 (manuscript received 5 Oct 94) pp 29-33

[Article by M. E. Eremeeva, V. F. Ignatovich, I. A. Nedvetzkaya and N. M. Balayeva, Epidemiology and Microbiology Scientific Research Institute imeni N. M. Gamaleya, Russian Academy of Medical Sciences]

[FBIS Abstract] The purpose of the study was the antigenic analysis of Rickettsia prowazekii, the obligate intracellular bacterium causing typhus fever in humans. Five strains of Rickettsia prowazekii different in origin, biological and genetic properties were compared with respect to protein and LPS patterns by the polyacrylamide gel electrophoresis method and the antigenic properties were studied by immunoblotting using specific sera of infected white mice. The three virulent strains — Breinl, G and Katsinjan — had identical protein patterns and differed from the isogenous pair of strains E and EVir with respect to the electrophoretic properties of 29-30 kDa proteins. Silver-stained LPS patterns were different in the five compared strains. Polyclonal mouse antisera contained specific antibodies which were directed mainly against the LPS and the 25-60 kDa proteins. The E and EVir strains were identical in all the performed immunoblotting reactions and were separated from the three virulent strains. Among the virulent strains, the whole cell antigen of the Katsinjan strain and the LPS antigen of the G strain had different reactions in comparison with the corresponding antigen of the standard Breinl strain. Figures 4; references: 33 Western.

Simple Method for cDNA Amplification Starting From Small Amount of Total RNA

957A0750D Moscow MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 6, Nov-Dec 94 (manuscript received 14 Apr 94) pp 38-40

[Article by G. A. Launer, K. A. Lukyanov, V. S. Tarabykin and S. A. Lukyanov, Bioorganic Chemistry Institute imeni M. M. Shemyakin and Yu. A. Ovchinnikov, Russian Academy of Sciences]

[FBIS Abstract] Existing methods for cDNA preparation for PCR require a quantitative removal of the T-primer excess after the first strand synthesis. If not removed, the primer undergoes oligo(dG)tailing and is amplified with a high efficiency, generating the primer dimer. A more

effective amplification of short cDNA sequences, resulting in enrichment of the sample with short molecules, is the other serious problem of this approach. It was proposed earlier that this difficulty could be circumvented by additional amplification of fractionated amplified cDNA, but this appears to be a complication of the method. The PCR-based method which is proposed in this article makes possible circumvention of both these difficulties. This new simple technique for the construction of cDNA libraries starting from small samples of cells or tissues is described. This technique is based on the insertion of inverted terminal repeats (ITR) into amplified cDNA, which causes a part of the molecules to generate "pan"-type structures in each cycle of PCR amplification. This makes it possible to avoid generation of the primer dimer and on the other hand makes possible the regulation of the average length of amplified sequences varying in the concentration of primers. Figures 3; references: 8 Western.

Reasons and Risk Factors for Infant Mortality in Several Uzbekistan Oblasts

957A0631A Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 6, Nov-Dec 94 (manuscript received 11 Nov 1992) pp 25-27

[Article by M.U. Nizamova, L.A. Tarasenko, and M.M. Yunusova (Research Institute of Pediatrics, Ministry of Health, Republic of Uzbekistan)

[FBIS Translated Text] Infant mortality is a multifactor problem which remains urgent up to the present time, and a wide circle of specialists is being attracted to its solution. Medical organizational factors are a substantial resource for reducing infant mortality.

In order to study the possibility of offering preventive and treatment care to babies living in rural regions, we analyzed the infant mortality indicators in the Surkhandarinsk and Syrdarinsk Oblasts of the Republic of Uzbekistan (1991, 41.2 and 47.9 percent per 1,000 live births).

In order to determine the true reason for the death of each baby, an expert analysis was done of primary material (family history and newborn development, medical history, and developmental history of the baby).

It was established that 37.8 percent of the women had chronic or acute extragenital illnesses. More than 50.0 percent of the women were anemic.

The babies of 63.5 percent of the women suffering from extragenital associated pathologies were born with symptoms of a perinatal pathology.

A perinatal pathology was recorded in 42.6 percent of all newborn babies hospitalized into pathology section (23.7 percent of the newborns died). More than 60.0 percent of the babies who died in the neonatal period were born prematurely. The premature babies frequently were babies born with extragenital and associated pathologies who were second-fourth in birth order. The syndrome of respiratory disorders occupied a dominant place in the composition of perinatal pathology (20.3 percent). In the newborn pathology section, pneumonia and ORVI [expansion not given] became the reason for the death of about 50.0 percent of the babies, 18.5 percent as the result of intracranial birth trauma, and 3.8 percent from anomalous birth defects. The scope of the investigation of these babies in the section was incomplete, and the treatment was insufficiently skilled.

In a study of the history of the development of the baby, it was established that 58.3 percent of the deceased babies belonged to the "in jeopardy" and "high risk" group from the moment of their birth; however, a negligible number of babies who had received health improvement treatment were included in the dispensary record. The regional doctors irregularly observed the babies for the first year of life; the notes of the doctor and the medical nurse on the history of the development of the baby as a rule, were formal, uniform, standardized, and did not reflect the dynamics of the state of health of the baby, or the physical and psychomotor development; there were no recommendations for proper nutrition or the prevention and treatment of background diseases: 79.3 percent of the babies who died afterward had ORVI (29.7 percent), pneumonia (19 percent), acute intestinal disease (16.2 percent), and of them, 24.7 percent of the babies fell ill 3-4 times. In this case, only one-fourth of these children were hospitalized in the hospital, and the remaining received ambulatory treatment.

Ambulatory treatment of 80.0 percent of the babies did not provide sufficient examination and skilled treatment. The regional doctors observed the babies irregularly and inopportunely during the period of the illness. The healthy babies also did not receive skilled and timely care from the home-visit nurses.

As the result of the low level of home-nurse observation of the healthy babies and treatment of sick babies, the indicators of home death of children are high (11.3 percent).

The high birth rate, the large number of children, and the low hygienic culture are the reasons for untimely seeking of medical care by parents and also the hospitalization of the sick baby. In addition, the parents frequently refuse hospitalization of the sick baby. All this explains the high level of perinatal mortality (26.5 percent). More than 50 percent of the babies who died in the first 24 hours of hospitalization were admitted in

a serious condition, and one-third of sick babies were admitted in an extremely serious condition.

It was established one-fourth of the babies who died in the hospital received only a partial examination. In the majority of cases examination was not done because of the serious condition of the baby or the short time the baby was in the hospital (39.2 percent), the poor skill of the doctor (19.3 percent), underestimation of the seriousness of the condition (10.4 percent), and also because of the lack of the corresponding medical equipment.

In conducting the expert evaluation of the rendering of medical care to babies in the hospital, it was established that 34.3 percent of the babies received skilled and timely treatment, 22.5 percent received poorly timed treatment, and 43.2 percent received insufficiently skilled treatment. The low level of hospital treatment is due to the inefficient use of antibiotics, insufficiently intensive therapy, inadequate resuscitation measures, and premature cessation of treatment.

Pathological-anatomical dissection was carried out in 13.0-14.0 percent of the cases, and the pathological-anatomical diagnosis completely confirmed the clinical diagnosis, without consideration of the inherent specifics.

In carrying out a comparative analysis of the outpatient and hospital diagnosis, it was observed that the greatest discrepancy was found in the directed diagnosis "acute respiratory illness," which outpatient physicians frequently diagnosed in children not having clinical symptoms. The outpatient diagnosis "acute intestinal illness" coincided with the hospital diagnosis in 67.7 percent of the babies.

The principal reasons for infant mortality were diseases of respiratory organs (40.8 percent), infections-parasitic diseases (35.2 percent), and perinatal pathology (18.3 percent).

A study of infant mortality from the "prevention" position made it possible to identify the characteristic deficiencies of the pediatric medical service, and to develop basic measures directed at reducing mortality. Data on the deceased babies were distributed according to preventability criteria: preventable, 70.3 percent; not preventable, 15.2 percent; preventability difficult to decide, 14.5 percent. In an analysis of data on the deceased babies which takes their age into account, it was established that the maximum of preventable death outcome is observed in the 1-6 month age group, and in the postnatal period, death is preventable in 74.0-77.0 percent of cases. Diseases of the respiratory organs occupy first place in the composition of preventable death outcomes, and infectious parasital diseases and several reasons for the origination of perinatal pathology are second.

Therefore, the campaign to reduce infant mortality should be organized at all stages of the rendering of medical care to babies, beginning with the improvement of hygienic conditions of mothers during pregnancy, and improvement in outpatient and hospital care. It is necessary to pay special attention to the preventive work or ambulatory outpatient institutions. It is advisable to conduct home visits for newborns and children differentially according to group health. Special attention should be paid to teaching mothers the correct care, nutrition, and nurturing of children of the age group. Each visit of the medical worker for the purposes of preventing illness must become for the mother an opportune school for the education of the child.

It is necessary to raise the quality of diagnostics and treatment at the hospital treatment stage. It is necessary to expand the network of children's hospitals in order to bring hospital care to the population.

Constant timely increase of the skill of physicians and allied health workers and their participation in the rearing of children in the first year of life also promotes an increase in the quality of the pediatric medical service.

Organization of a Center for a Specialized Course in Ambulatory Care

957A0631B Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 6, Nov-Dec 94 (manuscript received 19 Jan 93) pp 47-49

[Article by T.S. Soliyev, A.A. Ayubov, and Z.T. Tursunkulova]

[FBIS Translated Text] In 1991 the Ministry of Public Health of the Republic of Uzbekistan recommended the organization of a center for a specialized course in ambulatory care, SKAL, based on oblast, republic, and city multidisciplinary hospitals. The primary objective of the organization of such centers is to intensify the diagnosis and treatment process and to raise the quality of treatment of patients.

The SKAL center is governed by the local public health agency (according to the administrative line of authority) and the department of the medical institute or the scientific-research institute which provides scientific and organizational leadership. Patients with the most prevalent chronic noninfectious diseases of the internal organs and who have maintained mobility received treatment at such a center. The centers can function

both as part of a consolidated hospital and as a self-contained institution, which is this case has the status of a specialized hospital with outpatients.

The most prevalent illnesses in this region and the presence of specialists ready to treat these illnesses determine the profile of the center.

The basic tasks of the SKAL center are:

the provision of skilled care to patients which is directed by doctors of the outpatient facilities at the center corresponding to illness profile;

the examination of patients using modern diagnostic methods;

the provision of methods and consultation assistance to doctors having a public health practice;

the provision of a specialized course in ambulatory treatment, and, if necessary, short-term hospital treatment;

the organization of continuity between CKAL centers and outpatient clinics.

The CKAL center is a specialized ambulatory-inpatient complex with a single diagnosis and treatment unit which has a level of equipment corresponding to modern requirements. The activity of the center is financed within the framework of the budget of the public health departments.

The time required for the treatment of a patient depends on the seriousness of the pathological process. The patients are treated until a stable improvement is reached in 3-4 months. A detailed discharge paper with the history of the illness, and which includes further recommendations for further observation by a doctor at the place of residence, is given to the patient who has undergone a course of treatment. If necessary, the patient may undergo a second course of treatment at the SKAL center.

An admission sheet is given to the patient in the outpatient clinic according to the place of residence and is extended upon the recommendation of a clinic doctor.

The ambulatory department is the prominent component of the center. The following actions are performed in the department:

the establishment of indications for treatment of patients at the center;

the organization of consultations for patients not having indications for treatment at the center;

the treatment of each patient by one physician during a course of treatment;

the development of an integrated program of examination and course of treatment for each patient;

the identification of the possibility of the designation of certain treatment procedures in the outpatient clinic according to the place of residence;

the recording of the history of the illness of each patient on a single form;

the continuity of the center with the hospital and its constituent subdivisions;

the control of the course of the fulfillment of the planned diagnosis-treatment measures in the hospital;

the organization of consultations for patients who do not have indications for long treatment at the center, and the distribution to them of recommendations concerning the course of further treatment;

the formation of groups of patients for whom long observation and treatment at the center is indicated.

The admission of the patient to the center is accompanied by the filling out of a single (for ambulatory and hospital) history of the illness which includes first name, patronymic, and surname of the specialist accepting the patient for treatment. A treatment chart is given to the patient which indicates a number and the date the history of the disease was taken, the diagnosis of the patient, the medicines being taken, and physical procedures received, the surname of the doctor, and the telephone number of the registry office. The history of the illness, in which the indicated data are recorded are transferred to the office of the chief physician.

At the time of the first admission the doctor identifies the existence of illnesses for which the patient came for treatment at the center, predicts (when possible) the level of mobility of the patient in the next 5-6 months. If necessary, a comprehensive examination of the patient is carried out by means of modern diagnostic methods. The frequency of repeated visits is determined by the seriousness of the period of illness (on the average not more rarely than once every 10-12 days). When examination and treatment are not possible under ambulatory conditions (exacerbation of the illness, the danger of possible complications, the conducting of individual examination), the patients is hospitalized for a short period (up to 10 days) in the hospital. After release of the patient from the hospital, treatment is continued under ambulatory conditions. A brief transfer secondary crisis is formulated in which the character of the examination and treatment received in the hospital is presented in order to carry out further treatment in the ambulatory center. On the day of discharge of the

patient, the history of the illness is transferred to the chief physician of ambulatory medicine.

In accordance with the Ministry of Public Health of the Republic of Uzbekistan Health Order No 612 of July 1991 based on the clinic of the Second TamMY [expansion not given], a SKAL center for arthrology was founded for treatment of patients with rheumatoid arthritis, gout, Bekhterev disease, deforming osteoarthrosis, and reactive arthritises. In order to establish the clinical diagnosis of all patients, a complete blood analysis and biochemical analyses were studied, and if necessary, X-ray pictures of the joints and vertebrae, EKG's, and FKG's (expansion not given] were done. After establishment of a clinical diagnosis, in addition to medicinal treatment, acupuncture, physical therapy procedures, massage, therapeutic physical culture, hyperbaric oxygenation, and laser therapy were carried out. If necessary, intraarticular administration of medications and extracorporeal methods of treatment were used. Since June 1992 a SKAL center on this basis has been open for gastroenterology for patients with chronic gastritis, ulcers, chronic cholecystitis, chronic hepatitis, cirrhosis of the liver, chronic enterocolitis, and chronic pancreatitis. In order to make the diagnosis more precise, fibrogastroscopy, ultrasound, and radiological investigation have been used in addition to general clinical analyses. Ambulatory treatment has included physical procedures, massage, and LFK [expansion not give. Laser therapy was used to treat ulcers.

When necessary (upon the recommendation of faculty specialists), the patients has been hospitalized (for 3-10 days) in the specialized department. After discharge the patients have continued treatment ambulatorily. The total course of treatment is 3-4 months.

Assistants, docents, or professors have been consulted for all patients (upon the recommendation of the attending physician).

In an analysis of the work of the SKAL scientific centers, it was established that in 1992, 9,694 patients were treated by the arthrology department, 4,939 patients by the rheumatology department, and 2,604 patients by the gastroenterology department (from June to December, 1992). Due to the long observation with improvement and achievement of complete remission, 394 patients with deforming osteoarthrosis, 255 patients with rheumatoid arthritis, 70 patients with gout, 70 patients with reactive arthritis, and 40 patients with Bekhtereva disease were discharged.

In 1991 (before the organization of SKAL centers) for an indicator such as any day on the average, the rheumatology department had 23.3 patients; in 1992, due to the organization of the SKAL, 18.3, and in the first quarter of 1993, 17.3.

Therefore, SKAL centers are a new progressive form of specialized medical care for the population and are effective medically, socially and economically.

Epizootiology of Plague in Kyzylkumy

957A0631C Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 6, Nov-Dec 94 (manuscript received 4 Apr 92) pp 47-49

[Article by I.F. Melnikov and T.R. Radzhapov, Uzbek Antiplague Station]

[FBIS Translated Text] The epidemiology of plague is closely related to its epizootiology. Data on the characteristics of the manifestation of epizootic diseases of plague in Kyzylkumy are presented in order to describe the degree of threat of possible epidemic complications.

The self-contained focus of plague in Kyzylkumy occupies a territory of 33 million hectares, of which 16 million hectares falls within the territory of our republic [Uzbekistan].

The large peschanka [great gerbil, Rhombomys opimus Lichtenstein is the principal carrier of plague in this focus. The ecology and pathogenesis of the large peschanka is the main reason for the phenomenon of the natural home of plague. Numerous facts about the appearance of epizootic diseases and the predominant isolation of cultures from this species of rodents indicate this in particular. The large peschanka is a nidus species in Kyzylkamy. It comprises a nucleus of a certain group of animals to which are added close interrelationships and frequent parasitic contacts with noontime and red-tailed peschankas, the thin-fingered suslik, some three-fingered jerboas, the weasel, the white weasel, and other animals which have a second-degree significance in the role of plague carriers.

About 50 species of fleas have been observed in Kyzylkumy. Fleas of the family Xenopsylla, which are year-round parasites of the large peschanka, and also fleas of the families Coptopsylla, Nosopyllus, Paradoxopsyllus, which fulfill the role of carrier of plague in the autumn and winter, are the principal transferrers of plague in this nidus.

In carrying out epizootiological research on Central Kyzylkumy (1951-1991) it was observed that epizootic diseases of plague in the last 40 years have not appeared only in the years 1956-1960, 1976-1978, and 1985-1988. In 1951-1955 epizootic diseases of a different intensity appeared in the whole southern half of Central

Kyzylkumy and in the south up to the latitude of the settlement of Gazel. The intensity of the epizootic increased from the spring of 1952 and reached a maximum in the summer and spring of 1953[3]. Up to 1953 the area of epizootic reached 2 million hectares. Epizootic diseases were most acute in the spring and early summer in the population of the large peschankas, the number of which ranged within wide limits per year (an average of 5-10 animals per hectare, and a maximum of 29 individuals per hectare). A large population of fleas was noted everywhere. In the period indicated, 196 strains of pathogens of plague were isolated from rodents and fleas. The infectiousness of the large peschanka from the number of those investigated comprised 0.08-0.9, and of the fleas, 0.001-0.6.

The epizootic diseases of plague were recorded each year in Central Kyzylkumy from 1961 to 1975. The epizootic process among large peschankas occurred asynchronously in different parts of the desert and was characterized by different durations; however, it appeared in vast territories, successively migrating from the northernmost territories to the southern[2]. Epizootic diseases were recorded in West, Central, and South Kyzylkumy on the edge of the desert and in the oasis zone of several rayons of the Bukharskiy Oblast. The area of the epizootic in different years comprised from 1.2 million hectares to 8 million hectares (1967). In this period 2,141 strains of plague microbes were isolated from carriers and transferrers. The epizootic diseases appeared on a nidus of a great number of large peschankas (10-20 individuals per hectare) and in populations with a low number of rodents (1-2 specimens per hectare), but with a large population of fleas. Epizootic diseases were most intensive in spring (March - May) and in autumn (October - November). However, isolation of the plague pathogen was recorded in summer (July - August) and in winter. Thus, excavation of colonies of large peschankas which were done in January-March of 1970[1] when temperatures were below freezing showed that epizootic diseases also do not disappear in winter. With a large peschanka population of 0.2-0.5 per hectare, their activity is weak on the soil surface, and with stores of 239 to 573 specimens of fleas per colony, 0.3 percent of the infested animals and 1.9 percent of infected fleas were observed, and 48 cultures of the plague microbe were isolated.

Successive activation of the epizootic process of plague in Kyzylkumy was noted in 1979-1984. Epizootic diseases appeared especially intensively in 1980-1982, encompassing a territory of 6.5 million hectares (1981) in Central and South Kyzylkumy. In 1983 a drop in epizootic activity was noted, and by autumn 1984, they ceased everywhere. Epizootic diseases occurred on a nidus of a relatively high population of large peschankas (3-5 specimens per hectare), and in places, their population reached 15-30 animals per hectare. The flea population was also high. In this epizootic, the infectiousness with plague of large peschankas in different areas (vicinity of the settlement of Tamdy, the cities of Uchkuduk, Zarafshan, and the terrains of Altakyr, Kuntay, Kyzylkuduk, and others) comprised 5.0-6.0 percent, and of fleas, 10.0-36.0 percent. It should be noted that from spring 1982 to spring 1984 epizootic diseases appeared for the first time in the history of the investigation of Kyzylkumy when more than 600 cultures of the plague pathogen were isolated in the Karshinskiy and the Sundukli and Karnabchul sands. The large population of rodents in Sundukli is due to their high infestation with the territorial limitation of the epizootic localities. The red-tailed peschanka, the population of which has always been high, as well as the large peschanka, was involved in the epizootic diseases in the Karshinskiy Steppe. In all, from 1979-1984, 2,368 strains of the plague microbe were isolated from rodents and their fleas. From autumn 1984 to 1988 in Central Kyzylkumy a definite depression in the population of carriers and transferrers and the disappearance of epizootic diseases of plague in their populations were noted.

Table 1

Isolation of Cultures of the Plague Pathogen From Mammals

Mammal Species	Number of Strains of the Plague Microbe
Large Peschanka	1745
Noontide Peschanka	262
Red-tailed Peschanka	197
Combed Sand Peschanka	2

Isolation of Cultures of the Plague Pathogen From Mammals

Mammal Species	Number of Strains of the Plague Microbe
Yellow Suslik	5
Thin-fingered Suslik	4
Small Jerboa	1
Shaggy-legged Jerboa	9
Liechtenstein Jerboa	5
Severtsov Jerboa	1
Blind Rat-Mole	1
Tolay Hare	1
Fox	3
Tartar Fox	1
Camel	4
Domestic Cat	1
TOTAL	2242

Table 2

Isolation of Cultures of the Plague Pathogen From Ectoparasites

Ectoparasite Species	No. of Strains Isolated	Ectoparasite Species	No. of Strains Isolated
X. gerbilli	949	Rh socia	25
X. hirtipes	898	Rudaca	5
X. conformis	302	St. conspecta	14
X. skrjbini	3	St. vlaslovi	13
X. magdalinae	1	M. encta	3
Xenopsylla sp.	14	S. pallidus	1
C. lamellifes	189	P. irritans	1
C. bairamaliensis	9	Undetermined Fleas	989
C. olgae	3	H. asiaticum	22
N. tersus	211	o. tartakowskyi	9
N. laeviceps	112	Yxodidae	13
N. turcmenicus	27	Gamasidae	11
N. trispinus	3	Undetermined ticks	21
P. teretifrons	37	Lice	4
Ct. dolichus	10	TOTAL	3912
Rh. cedestis	23		

A successive cycle of epizootic activity in Central Kyzylkumy began in the spring of 1989. The intensity of the epizootic sharply increased in 1990-1991, encompassing a territory of 0.5 million hectares. In regard to the fact that all conditions exist for transmission delivery of the pathogen, the epizootic has the tendency for further intensification and further spatial migration. In 1989-1991, 269 cultures of the plague microbe were isolated, including 73 from rodents and 169 from fleas.

Tables 1 and 2 present the results of the isolation, (1951-1991) of the plague pathogen in Central Kyzylkumy from mammals and their fleas.

It is apparent from Table 1 that 97.2 percent of the cultures isolated are from the four species of peschanka, and of these, 77.8 percent are from the large peschanka, and this confirms the leading role of this mammal as the principal carrier of plague. It should be emphasized that the isolation of the plague microbe from wild fur-bearing animals (foxes, steppe foxes, and hares), camels and domestic cats has great importance for the epidemiology of plague.

Cultures of the plague microbe have been isolated from 23 species of fleas and four families of ticks (Table 2). In autumn and winter a number of strains were isolated from fleas of the family Xenopsylla (55.6 percent), which as the principal transferrer of plague, and massive species of fleas were isolated from Coptopcylla and Nosopsyllus (14.4 percent).

Thus, it is possible to conclude that in the 40 years of investigation of Kyzylkumy, it is one of the most active natural foci of plague.

The development of epizootic diseases and their activity and intensity regularly appear in areas with an increased population of the large peschanka (5-15 individuals per hectare). However, after intensive epizootic diseases (November-May) during which the population of large peschankas basically is sharply reduced (0.5-3 per hectare), epizootic diseases disappeared.

The population of fleas of the family Xenopsylla (in addition to the usual seasonal changes in the population during the year) also was practically stable in the territory with a stable population of the large peschanka. In places where rodents became extinct, after timely abundance of fleas which migrated from the burrows, their population markedly decreased.

In areas of the development of epizootic diseases, the latter were observed for a period of 2-3 seasons. In the 1.5-2 years following the beginning of the epizootic diseases, depression of the rodent population intensified, and the plague microbe was isolated from rodents and fleas only in individual cases, only under conditions especially favorable for sick peschankas (observation of the pathogen during continual hunting of these colonies).

For 30 epizootic years in Central Kyzylkum an export of the plague pathogen from the northern territories with subsequent migration of epizootic diseases in the southern and eastern directions[2] and spontaneous appearance of the epizootic processes in the west and south (1979-1984), with their subsequent distribution to the south and east, has been observed.

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De Novo Design of Sequence-Specific DNA-Binding Peptides Using the Motif β Strand-Turn-β Strand To Recognize a Nucleotide Sequence on DNA

957A0479A Kiev TSITOLOGIYA I GENETIKA in Russian Vol 28 No 6, Nov-Dec 94 (manuscript received 14 Jul 94) pp 1383-1399

[Article by A.N. Surovaya, S.L. Grokhovskiy, R.V. Brusov, Yu.P. Lysov, A.L. Zhuze, and G.V. Gurskiy, Molecular Biology Institute imeni V.A. Engelgardt, Russian Academy of Sciences, Moscow; UDC 577.323]

[FBIS Abstract] The solid-phase synthesis method was used to design de novo and manually synthesize linear and cyclic 26-unit peptides that use a β strand-turn-lb strand motif for recognition of nucleotide sequences on DNA. The amino acid sequences in the said peptides are identical; however, the structure of the cyclic peptide is constrained by the presence of S-S bonds between the cysteine radicals. A 28-unit peptide was also synthesized, the N-terminal of which contains a Gly-Gly-His tripeptide capable of chelating a copper ion. It may serve as a potential DNA-cleaving reagent. Amino acid analysis yielded the following data (in mole fractions) for the three peptides (the numbers in parentheses are the theoretical values of the mole fractious conforming to the peptide's chemical structure): Peptide 1: Asp 1.42 (1), Thr 5.14 (5), Gly 3.99 (4), Ala 1.00 (1), Val

4.22 (5), Leu 1.23 (1), Lys 6.48 (6); Peptide 2: Asp 1.13 (1), Thr 4.77 (5), Gly 5.69 (6), Ala 1.18 (1), Val 5.15 (5), Leu 1.44 (1), His 0.86 (1), Leu 5.90 (6); and Peptide 3: Asp 1.21 (1), Thr 5.02 (5), Gly 4.39 (4), Ala 0.92 (1), Val 4.72 (5), Leu 1.00 (1), Lys 6.56 (6). The binding of these peptides with natural DNA, an individual restriction enzyme fragment, and synthetic polydeoxyribonucleotides was studied by a variety of physicochemical methods, including circular dichroism [CD] spectroscopy, fluorescence methods, and DNase I footprinting. The CD spectroscopy studies demonstrated that the 26-unit linear and cyclic peptides are in a disordered conformation and partially in a β conformation in an aqueous solution and in the presence of 20 percent 2,2,2-trifluoroethanol [TFE] but that they assume a partially α-spiral conformation in 50 percent TFE. The linear and cyclic peptides were demonstrated to bind with DNA. The complexes approach saturation if one molecule of the peptide is bound per three-four pairs of DNA base pairs. It was also discovered that the antibiotic distamycin A, which binds in the minor DNA groove, competes effectively with the linear and cyclic peptides for the binding sites poly(dA)poly(dT). The CD spectroscopy studies also established that the molecules undergo conformation changes upon binding, whereas the structure of the DNA remains largely unchanged. The difference CD spectra obtained by subtracting the spectrum of the free DNA from the spectrum of the peptide plus DNA mixture was different than the spectrum of the free peptide. The form of the difference CD spectra was consistent with transition of the peptide from a disordered conformation into a β-like conformation upon its binding with DNA. The DNase I footprinting diagrams confirmed the presence of specific protection of the nucleotide sequences by linear and cyclic peptides at the periphery of the operators O_R1, O_R2, and O_R3 and pseudo-operators in the vicinity of the *cro* gene of the phage 434. Figures 10, tables 2; references 49: 6 Russian, 43 Western.

New Method of Comparative Analysis of Gene Expression and Identification of Differentially Expressed mRNA

957A0479B Kiev MOLEKYLYARNAYA BIOLOGIYA in Russian Vol 28 No 6, Nov-Dec 94 (manuscript received 8 Jul 94) pp 1367-1382

[Article by N.B. Ivanova, I.V. Fesenko, and A.V. Belyavksiy, Molecular Biology Institute imeni V.A. Engelgardt, Russian Academy of Sciences, Moscow; UDC 577.214]

[FBIS Abstract] A new approach to comparative analysis of the expression of genes has been proposed. According to the proposed procedure, the set of messenger RNA [mRNA] sequences is represented in the form of a set of discrete restrictase fragments of complementary DNA [cDNA]. Then, selective isolation of the 3'-terminal fragments is performed so that each form of mRNA will be represented by no more than one fragment having a characteristic length and sequence. Sets of cDNA fragments of different types of cells are divided by high-resolution polyacrylamide gel electrophoresis and compared. The proposed approach was used to identify and clone fragments of two genes demonstrating differential expression in the thymus and spleen of mice of the line C57B16. The primary splitting of the double-stranded cDNA was performed by using the restriction enzyme *Sau*3AI. For the sake of comparison, the restriction enzyme *Bam*HI was also used to split the cDNA. The restrictases *Eco*RV, *Pst*I, *Msp*I, and *Hin*PI were used to release the labeled subfragments from the immobilized cDNA fragments. Bands specific for each of the two organs were visible in the autoradiogram of the electrophoretic separation of the labeled thymus and spleen cDNA fragments. Each secondary restriction enzyme yielded a characteristic, unrepeated set of fragments. Furthermore, use of the second restriction nuclease, i.e., *Bam*HI, for the primary splitting yielded a different pattern of fragments, thus providing additional evidence of the specificity of the proposed approach. Approximately 11 percent of the fragments of thymus cDNA and 8 percent of the fragments of spleen cDNA were differential, which is to say that they gave off a signal that was at least three times stronger in one organ than in the other. This was consistent with the level of differences in the composition of mRNA of various mammalian tissues (on the order of 10 percent). After the fragments of the two genes were identified, they were cloned. One of the two genes was established to code terminal deoxynucleotidyl transferase. The second gene was detected for the first time. The proposed approach's advantages and limitations were discussed. One limitation mentioned was the fact that mRNA sequences may be found that do not have suitable hydrolysis sites. A computer analysis of all known sequences of murine cDNA having a completely sequenced 3'-terminal (659 sequences) was performed to determine the extent to which the said limitation would restrict the proposed method's suitability. It was determined that when the *Sau*3AI is used for the primary splitting, sequences were split by the said enzyme at a distance from the 3'-terminal not exceeding 1.0 to 1.5 kb. With secondary splitting of the resultant 3'-terminal set of enzymes, more than 96 percent of the said population may be split by using 10 different restriction endonucleases with four-letter recognition sites. That figure may be raised to 100 percent if a restriction site at which several percent of the remaining enzymes can be split

offis added to the T-primer. It was further stated that because the method does not entail a stage of hybridization involving an extremely complex mixture of fragments with greatly differing degrees of representativeness, it permits a significant lowering of the threshold of detecting differentially expressed sequences. Figures 3; references 14 (Western).

Protein Chain Can Achieve Energy Minimum Without Exhaustive Sorting of All Its Conformations: Computer Simulation and Phenomenologic Theory

957A0479C Kiev TSITOLOGIYA I GENETIKA in Russian Vol 28 No 6, Nov-Dec 94 (manuscript received 22 Nov 93) pp 1412-1427

[Article by O.V. Galzitskaya, B.A. Reva, and A.V. Finkelshteyn, Protein Institute, Russian Academy of Sciences, Pushchino, Moscow Oblast, and Mathematical Problems in Biology Institute, Russian Academy of Sciences, Pushchino, Moscow Oblast; UDC 577.322]

[FBIS Abstract] A simple model describing bilayer β-proteins was used to perform a Monte Carlo method study of how a protein achieves its lowest energy state. The model, which was proposed in two previous publications by the authors of the present study, describes only the globular state (i.e., only the secondary structure of the globule) and ignores the more numerous turned and semiturned conformations of the chain. The model was said to correspond not to a "solid" native protein but rather to a "melted down" globule whose side groups would have become "unfastened" but whose main chain would have retained the major part of its architecture. The "protein" was assumed to consist of six β-segments that each lay on its own "directrix." Together, the "directrixes" form the globule's three-dimensional lattice. Each directrix includes seven positions, and each β-segment may consist of five, six, or seven amino acid radicals. The end positions of each directrix may be occupied by β-structure radicals or unoccupied. The β-sections are connected by loops consisting of three or more radicals. As a result, the total number of states in the model is 44,032 with a chain length of 54. The kinetics of the chain's conformation changes were studied by the Monte Carlo method based on a standard Metropolis algorithm. In addition to the numerical experiment, a series of kinetic experiments were performed. Ten random sequences were created. The kinetic curve of the change in energy at T = 300 K was presented for one of the sequences. It was demonstrated that at T = 300 K, the chain reaches its lowest energy state within approximately 10^3 Monte Carlo steps, which is very quick in comparison to the time required for exhaustive sorting of all of its 44,032 conformations. To clarify the temperature dependence of the characteristic time required for a global energy minimum to be achieved, the scientists performed 50 Monte Carlo experiments at various temperatures from 75 K to 1,000 K for each of the 10 random sequences. The maximum rate of attainment of a global energy minimum for the said chains was determined to be at temperatures of approximately 150 to 300 K. At lower temperatures, the rate at which the lowest energy state was achieved was limited by energy factors. At higher temperatures, it was limited by entropy factors. It was concluded that even for "random" sequences, there exists an optimum temperature range within which the energy minimum is found quickly without exhaustive sorting of all of a chain's conformations. The optimum range for finding the minimum energy was further shown to be determined by the critical temperature characteristic for the onset of "freezing out" of the lowest-energy folds of the protein chain. A simple phenomenological model was presented to account for the protein chain's behavior. Figures 10, tables 2; references 32: 3 Russian, 29 Western.

Temperature Reaction of Rabbits to Local Effects of Microwaves

957A0747A Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KULTURY in Russian No 6, Nov-Dec 94 (manuscript received 6 Apr 94) pp 29-34

[Article by S. M. Zubkova, Ye. N. Streltsova, Ya. Z. Lyakhovetskiy, Russian Science Center for Rehabilitation and Physiotherapy, Ministry of Health and the Medical Industry of the Russian Federation, Moscow; UDC 612.591.15.882:092.9-06:615.849.112]

[FBIS Abstract] This paper studies vasomotor response to microwave radiation in the irradiation zone and periphery. The heart, thyroid gland, and thymus gland regions were studied. The question is posed of why rectal temperature remains constant in localized irradiation. The dependence of the changes in skin temperature on intensity and localization of irradiation and the initial state of the animal are studied. The role of central and peripheral nervous system formations is studied. There was a rapid increase in skin temperature immediately after the cessation of microwave irradiation and during the subsequent 20-30 minutes in the region of the heart and thyroid, a vasomotor response. Myocardial reactions and extracardial vegetative responses are detected when the heart and thyroid are irradiated, respectively. It is these reactions which may prevent tissue heating, resulting in a constant rectal temperature. Figures 7; tables 2; references 19: 4 Russian, 15 Western.

Ecological Situation in Recreational Areas in Urbanized Regions of the Central Volga and Urals

957A0747B Moscow VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KULTURY in Russian No 6, Nov-Dec 94 (manuscript received 20 APr 94) pp 37-39

[Article by G. V. Kulikov, Russian Science Center for Rehabilitation and Physiotherapy, Ministry of Health and the Medical Industry of the Russian Federation, Moscow; UDC 615.838:614.7].07]

[FBIS Abstract] Many of the vacation spots frequented by Russian citizens in the Soviet period now lie beyond Russian borders. These spots are now less accessible. The importance of local urban recreational areas is consequently greater. The current ecological state of recreational areas in the Central Volga region and Urals (Samara, Ulyanovsk oblasts and Bashkiria) was studied. Bashkiria has the greatest stress load on the environment. The water is polluted with nitrates, and the air with carbon monoxide, heavy solid particulate matter, hydrocarbons, and sulfur and nitrogen oxides. Heavy metals are found in the soil. Bashkiria has 12 sites which use mineral waters and muds for therapeutic purposes. All are in polluted regions, even those far from industrial centers. Samara's mineral waters have been polluted due to karst formation and the fracturing of water-bearing rock. Deep water-bearing strata are also oil-bearing strata which may be contaminated in oil exploration operations. The mineral water supplied in Ulyanovsk oblast are generally in good condition, but they are threatened by factors which hold true for all of the studied regions. There is no consideration of environmental protection in industrial and regional development planning, and environmental protection measures are insufficient or ineffective. Resources have not been surveyed and cataloged, so they may not be considered in regional planning. In addition, existing recreational sites are not taking appropriate environmental protection measures.

Daily Energy Expenditures and Energy Demand of Students in Schools of General Education in the Conditions of the Republic of Uzbekistan

957A0636A Moscow GIGIYENA I SANITARIYA in Russian No 9, Nov-Dec 94 pp 20-21

[Article by N. V. Voronina, Scientific Research Institute of Sanitation, Hygiene and Occupational Diseases, Ministry of Health of the Republic of Uzbekistan, Tashkent; UDC 613.731:613.955]-07]

[FBIS Translated Text] According to present ideas, energy demand is viewed as the amount of energy needed to maintain health, develop the body and support a socially desirable level of the individual's physical activity [2].

Climatic, social and biological factors have a significant influence on the energy demand of a child's body, which makes it necessary to periodically study the daily energy expenditures of children and adolescents with the goal of adjusting their physiological energy demand.

The research was conducted at Tashkent's schools of secondary general education in spring and fall. Schoolchildren of three age and sex groups were surveyed—7-10, 11-13 and 14-17 years.

The daily budget was studied on the basis of questionnaires over the course of 7 days in each season. An analysis was made of 1,297 time-and-motion charts.

Energy metabolism in different body positions and different forms of activity was studied by indirect calorimetry [1]. Air samples were subjected to gas analysis using a Spirolyt-II instrument (Germany). Examinations were made of students of average physical development falling into health groups I and II. We used experimental data on the energy cost of different activities of the students and the results of their daily time budget to calculate daily energy expenditures. To establish the physiological energy demand we increased the obtained daily energy expenditures by 10 percent [1].

The results of analyzing the daily time budget of schoolchildren are presented in Table 1.

Table 1. Daily Time Budget of Students of Schools of General Education (M +/- m)

Position and Form of Activity	Boys			Girls		
	7-10 Years	11-13 Years	14-17 Years	7-10 Years	11-13 Years	14-17 Years
Sleeping (resting lying down)	9 hr 51 min	9 hr 14 min	8 hr 52 min	9 hr 54 min	9 hr 20 min	8 hr 31 min
Sitting	8 hr 16 min	8 hr 40 min	9 hr 42 min	8 hr 30 min	8 hr 57 min	9 hr 25 min
Standing	58 min	1 hr 09 min	52 min	1 hr	1 hr 05 min	54 min

Position and Form of Activity	Boys			Girls		
	7-10 Years	11-13 Years	14-17 Years	7-10 Years	11-13 Years	14-17 Years
Walking	1 hr 24 min	1 hr 42 min	2 hr 04 min	1 hr 38 min	1 hr 53 min	2 hr 03 min
Walking on stairs	2 min	7 min	10 min	3 min	9 min	9 min
Running	30 min	21 min	10 min	28 min	16 min	7 min
Physical culture and sports	1 hr 51 min	1 hr 47 min	58 min	1 hr 20 min	1 hr 09 min	53 min
Personal hygiene and work	1 hr 09 min	1 hr	1 hr 12 min	1 hr 07 min	1 hr 11 min	1 hr 58 min

Sleeping takes up the largest share of the daily budget of schoolchildren (35-42 percent of the day). The duration of sleep decreased as the age of the students increased. The opposite pattern was observed in relation to activity in seated position. The duration of activity in seated position came to 34-41 percent in the daily time budget. The time devoted to activity in standing position was 3-5 percent of the day. According to published data, depending on the age and sex of children and adolescents, motor activity should take up 12.5-21 percent [3]. Analysis of the dynamic component of motor activity showed that it is within the limits of the hygienic norm (18.5-21 percent) for all age and sex groups.

In our opinion a sufficient level of motor activity for students requires increasing the length of physical culture periods and expanding the program of work for schoolchildren, foreseen by the reforms of schools of general education.

Table 2. Energy Expenditures of Students (kcal/min) in Different Body Positions and Different Forms of Activity Depending on Age and Sex, on a Yearly AverageM +/- m)

Position and Form of Activity	Boys			Girls		
	7-10 Years (n=16)	11-13 Years (n=12)	14-17 Years (n=16)	7-10 Years (n=16)	11-13 Years (n=12)	14-17 Years (n=16)
Sleeping (resting lying down)	0.91 +/- 0.06	1.0 +/-0.08	1.18 +/- 0.07	0.87 +/- 0.05	0.90 +/- 0.08	1.02 +/-0.06
Sitting	0.97 +/- 0.06	1.14 +/- 0.1	1.39 +/-0.09	0.96 +/- 0.06	0.99 +/- 0.06	1.17 +/- 0.07
Standing	1.08 +/- 0.07	1.18 +/- 0.1	1.39 +/-0.09	1.04 +/- 0.07	1.05 +/- 0.09	1.22 +/- 0.08
Walking	2.48 +/- 0.15	3.24 +/- 0.27	3.78 +/-0.24	2.26 +/- 0.14	2.84 +/- 0.24	3.25 +/- 0.20
Walking on stairs	2.98 +/- 0.19	3.85 +/- 0.32	3.9 +/-0.31	2.78 +/- 0.17	3.33 +/- 0.28	4.51 +/- 0.28
Running	4.59 +/- 0.29	5.57 +/- 0.46	6.56 +/-0.41	4.52 +/- 0.28	4.79 +/- 0.4	5.47 +/- 0.34
Physical culture and sports	3.1 +/- 0.19	4.16 +/-0.35	5.33 +/- 0.33	2.87 +/- 0.18	3.69 +/- 0.31	4.61 +/-0.29
Personal hygiene and housekeeping	2.07 +/- 0.13	2.56 +/-0.21	2.93 +/- 0.18	2.0 +/- 0.13	2.18 +/- 0.18	2.45 +/-0.15

Table 3. Actual Daily Energy Expenditures of Children and Adolescents and Their Energy Demand

Age Group, Years	Sex	Energy Expenditures, kcal/day	Energy Demand
7-10	Boys	1906.9 +/- 9.1	2100
	Girls	1789.2 +/- 7.6	1970
11-13	Boys	2280.6 +/- 10.9	2510
	Girls	1929.2 +/- 9.2	2120
14-17	Boys	2581.2 +/- 12.3	2840
	Girls	2250.0 +/- 10.2	2475

Data characterizing the energy expenditures of children and adolescents during different forms of activity are presented in Table 2.

Boys expended more energy than girls on a daily average in active forms of activity. Energy expenditures in the same forms of activity rise with increasing age; however, when energy expenditures are expressed per unit body weight, their amounts decrease with age. Daily energy expenditures increased with age (Table 3). In this case the energy expenditures of boys were significantly higher than of girls ($p<0.05$).

The results made it possible to substantiate the adequate energy value of the food rations of students of schools of general education in the Republic of Uzbekistan, and to create a sensible diet for them.

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Skin Wounds and Burns Contaminated by α-Emitters in Personnel of a Radiochemical Enterprise

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[Article by A. G. Bazhin, V. F. Khokhryakov and V. A. Shevkunov, Branch No 1, Institute of Biophysics, Russian Ministry of Health and Medical Industry, Chelyabinsk; UDC 617-001.17-02:613.648]-07]

[FBIS Translated Text] The literature contains information on cases of contamination of injured skin by plutonium among personnel of Russian [1,6] and foreign [2,7-9] atomic industry enterprises. In this case the victims suffered various skin injuries at work, chiefly to the upper limbs, with a significant proportion of the injuries being contaminated with a radionuclide [6-9]. The cited papers analyze plutonium metabolism, measures of specialized health care, and delayed effects when a wound is contaminated by plutonium.

The goal of this study was to evaluate, from the standpoint of radiation hygiene, recorded cases of skin injury among workers in different occupations employed in the main production sections of the Mayak Production Association, and to analyze the traumatizing factors, the frequency of cases, the location, nature and depth of skin injury, the levels of contamination of injuries by α-emitters, and the effectiveness of first aid measures.

The observation group consisted of 3,968 workers of the radiochemical enterprise who came in contact with insoluble and relatively soluble compounds of plutonium and americium-241 (^{241}Am). In cases of contamination of injured (or uninjured) skin, mandatory treatment (decontamination) was conducted at decontamination centers in accordance with currently effective instructions and recommendations [2,4-6], after which the victims were sent to a public health center. At the public health center, the wounds and burns were examined, and treated again as necessary, and pentacene was administered intravenously when so indicated. Then the victims were sent to a hospital for examination by a surgeon and for measurement of the level of superficial contamination and the quantity of plutonium and americium in the wounds.

The levels of superficial contamination of the skin surface by α-and β-emitting nuclides were measured by means of standard radiometric instruments—SPAR-1 and RUP-1, and beginning in 1981, by means of a set-up assembled out of standard blocks and devices. The quantity of α-emitters in wounds was measured on the basis of roentgen or soft γ-radiation accompanying α-decay, using a scintillation spectrometer, the lower radioactivity detection limits of which were 14 Bq for plutonium and 3 Bq for ^{241}Am.

The frequency of cases of contamination of injured skin was estimated with regard for occupation, place of work and the factors responsible for skin damage. We analyzed the nature, depth and location of wounds, and the severity of burns. Wound depth was determined tentatively on the basis of clinical signs and the results of a doctor's examination. When the depth of injuries was less than 1 mm, they were classified as epidermal (microtraumas—abrasions, scratches, "pricks"), when all dermal layers were injured (a depth greater than 1 mm), they were classified as dermal, and when the skin and underlying tissues (fasciae, muscles, tendons, down as far as the periosteum) were injured, they were classified as transdermal wounds. In addition we analyzed the times victims were sent and admitted (or referred) to the hospital, as well as detection of "old" injuries during planned medical examinations of personnel. The frequency of cases of injury was defined as the ratio of the number of workers with skin injuries to the total number of examined persons, in the entire observation group as a whole and separately in relation to different groups of specialists.

Between 1948 and 1992 the clinical department of the biophysics laboratory examined 3,968 workers of the Mayak Production Association with the goal of revealing contamination of injured and intact skin by plutonium and ^{241}Am. Various injuries to the skin contaminated chiefly by α-active radionuclides were discovered in 286 persons. The distribution of personnel with skin injuries in relation to the "traumatizing factor" criterion was as follows: Mechanical injuries (wounds) were recorded among 248 persons, chemical burns were recorded among 30, and thermal skin burns were recorded among 8, or respectively among 6.25, 0.76 and 0.20 percent of the total number of subjects. The overall frequency of injuries was 7.2 percent.

According to the results, 10 percent of surveyed workers came in contact with poorly transportable compounds of plutonium and ^{241}Am, 24.8 percent did so with relatively transportable compounds, but the bulk of the individuals (55.9 percent) had approximately identical contact with both types of radionuclide compounds; 6.7 percent of the workers were white collar workers or workers in auxiliary and construction organizations, and were not in constant contact with industrial plutonium compounds.

The frequency and forms of injury depended to a significant degree on working conditions and occupation. Among the surveyed specialists, skin injuries were experienced most often by foundry workers (28.1 percent) and turners (21.7 percent) working in the mechanical production section, and by machine operators of the chemical department (13.2 percent). These were chiefly mechanical injuries—wounds, the frequency of which was 27.1, 21.2 and 11 percent respectively for the indicated groups.

Cases of chemical skin burns were not recorded among foundry workers and turners. There were 10 victims with acid skin burns respectively among machine operators and among fitter-repairmen. Nitric acid solutions were the traumatizing factor of chemical burns among 28 persons, hydrochloric acid solutions were the traumatizing factor for one, and alkali was the traumatizing factor for one. Thermal skin burns were discovered among welders, foundry workers and turners coming in contact with hot metal.

A relatively high frequency of injuries was noted among combined groups of fitters (repairmen, mechanics, toolmakers, attendants)—6.5 percent, and engineers and technicians (process engineers, mechanical engineers)—5.3 percent, working in the main production sections. In other occupational groups, injuries were a rare phenomenon, and their frequency was from 1.1 to 3.8 percent. Injuries often occurred during repairs and preventive work. It should be noted that the frequency of cases involving contamination of skin injuries recorded at the Mayak Production Association does not differ significantly from the frequency of the same incidents among workers at similar enterprises abroad [2,7-9].

Information on the quantity and location of skin injuries is presented in Table 1.

Table 1. Type, Quantity and Location of Skin Injuries

Type of Injury	Number of Victims	Number of Injured Areas	Body Parts			
			Hands	Legs	Head and Neck	Torso
Wounds	248	349	332	7	9	1
Chemical burns	30	55	21	16	11	7
Thermal burns	8	11	7	2	2	-
Total	286	415	360	25	22	8

The relative frequency of cases of different injuries among injured workers (the "type of injury" criterion) was as follows: Mechanical skin injuries were diagnosed among 86.7 percent of the individuals, chemical burns were diagnosed among 10.5 percent, and thermal burns were diagnosed among 2.8 percent. In accidents (explosions of containers and flasks, spilling of solutions) the number of injured skin areas reached 9 on one victim. In addition some persons received skin injuries up to four times during the entire period of work, as a consequence of which 415 injured skin areas were recorded among 286 persons. The distribution of skin areas in relation to types of injuries, expressed as a percent of their total number, was practically the same as the distribution of victims.

Workers injured skin on the upper limbs, and mainly the fingers, most often (86.7 percent), while injuries were significantly rarer to lower limbs (6.0 percent), the head and neck (5.3 percent) and the torso (1.9 percent). This pattern is noted with all types of injuries. Such indicators have also been cited by other authors [1,8,9]. Information on injuries is presented in Table 2.

Table 2. Depth and Nature of Mechanical Skin Injuries

Depth of Injury	Nature of Injury					Total
	Puncture	Cut	Laceration	Gash	Other	
Less than 1 mm (Microtraumas)	34	22	31	-	16*	103
More than 1 mm (Wounds)	168	55	15	3	5**	246
Microtraumas and wounds	202	77	46	3	21	349

Note: *—cases recorded as superficial skin injuries; **—injuries include three crushing wounds and two contusions.

Analysis of the depth of skin injury established that 103 out of 349 wounds (29.5 percent) are epidermal, with injury occurring to the epidermis and the upper part of the papillary layer of the dermis (microtraumas); 227 (65 percent) were classified as dermal wounds, and 19 (5.4 percent) were classified as transdermal wounds. The last two types of injuries were combined into the "wound" group with a depth of tissue injury greater than 1 mm, because the full volume of specialized care must be rendered when they are contaminated by plutonium.

When classified by "nature of injury," 57.9 percent of the wounds were determined to be punctures, 22.1 percent were cuts, and 13.2 percent were lacerations.

Workers with transdermal wounds and the majority of victims with dermal wounds (195 persons, 55.9 percent) entered the hospital in the first 6-24 hours after injury; 64 (18.4 percent) of the wounds were revealed upon referral of victims after 7-14 days due to their poor healing or after a period of 1-2 months

to 2 years after injury in connection with development of pathological changes in tissues in the injured area. Ninety (25.9 percent) wounds were revealed during planned medical examinations of personnel at times from 1 year to 35 years after the incident. These were mainly epidermal wounds, with dermal wounds making up a small fraction.

Medical care was provided in the hospital over the course of 1 day. The needed volume was determined by measuring the activity of α-emitters in the wound. It should be noted that only those quantities of plutonium and ^{241}Am that remained in wounds after decontamination at work stations and in public health centers were measured in the laboratory. The concentration of radionuclides in 119 of 349 recorded wounds (34.1 percent) was at the lower limits of detection: for plutonium—14 Bq, for americium—3 Bq. Disregarding initial contamination, these skin injuries may be defined as "conditionally clean." Radionuclides with a total concentration of 14 to 74 Bq were discovered in 44 wounds (12.6 percent). All in all, the residual concentration of α-active nuclides in 163 wounds was below or at 74 Bq—the value recommended as permissible [6], based on the goal of protecting a critical organ (the skeleton), equal to 0.1 DS [not further identified] (DS ^{239}Pu) in the skeleton for personnel equal to 740 Bq [sic] [3]. Wound management was limited in such cases to additional processing and conservative treatment of the wounds.

Processing of wound surfaces in the hospital did not usually lead to a decrease in α-activity remaining after first aid. This fact may be explained by the fact that the effectiveness of initial multiple processing of wound surfaces with antiseptic solutions (3 percent hydrogen peroxide and 0.5 percent potassium permanganate) was high, and some of the radionuclides remained in the wounds, lodged firmly in necrotic tissues and inaccessible to decontamination. Radionuclide concentrations were from 75 to 740 Bq in 80 (22.9 percent) wounds, from 741 to 3,700 Bq in 41 (11.7 percent), and from 3,701 to 7,400 Bq in 43 (12.3 percent). In 22 cases the plutonium concentration in wounds was unknown because they were received in 1948-1958, when radiometric apparatus for its effective measurement was absent; only presence of contamination was noted. Wound plutonium concentrations in amounts exceeding 74 Bq were the grounds for prescribing specialized medical care in its full volume, to include processing and resecting the wounds or electrocoagulation of wound surfaces and complexon therapy. It was prescribed in all of the cases listed above (192), but for a number of reasons (refusal to undergo resection etc.), it was provided in full volume to 176 victims, and partially to 16. The latter included six persons with skin burns.

Twenty-five persons with skin burns were directed and admitted to the hospital 1 day after injury, 10 were admitted after 3-5 days, and injuries were detected among three persons during planned medical examinations. Burns were classified as follows by the "severity" criterion: 27.2 percent—1st degree, 42.4 percent—1st-2d degree, 25.7 percent—2d degree, 4.5 percent—3d degree. Thus superficial burns developed in 95.4 percent of the cases, which made possible prompt and effective treatment (decontamination) of burned skin at decontamination stations in accordance with the instructions [2], thus permitting prevention of injury to the papillary and reticular layers of the dermis.

Conclusions

1. The frequency of skin injuries among surveyed workers of the Mayak Production Association in the period from 1948 to 1992 was 7.2 percent. Injuries were contaminated by insoluble and relatively soluble compounds of plutonium and americium-241 (^{241}Am).

2. Four hundred fifteen injured skin areas were discovered among 286 persons with injuries, to include 84.1 percent mechanical injuries (wounds), 13.2 percent chemical burns (acid), and 2.7 percent thermal burns; 86.7 percent of the injuries were on the upper limbs, mainly on the fingers.

3. The residual concentration of plutonium and ^{241}Am in wounds detected by measurements made upon admission of workers to the hospital was below 74 Bq in 46.7 percent of the cases, and it exceeded this amount in 53.3 percent of the cases.

4. All victims had been given first aid. Timely removal of acid from skin surfaces made it possible to prevent development of deep burns in most cases (95.4 percent), while prompt processing of wounds in 34.1 percent of the cases led to a decrease in the levels of contamination to the background readings of the instruments. Specialized medical care was rendered to 192 workers (67.1 percent).

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Substantiation of a Criterion for Standardization and Comprehensive Evaluation of the Habitability of Military Equipment

957A0636C Moscow GIGIYENA I SANITARIYA in Russian No 9, Nov-Dec 94 pp 35-39

[Article by I. D. Kudrin, M. N. Tikhonov and V. V. Dovgusha, St. Petersburg; UDC 614.7.623.438.3]-074]

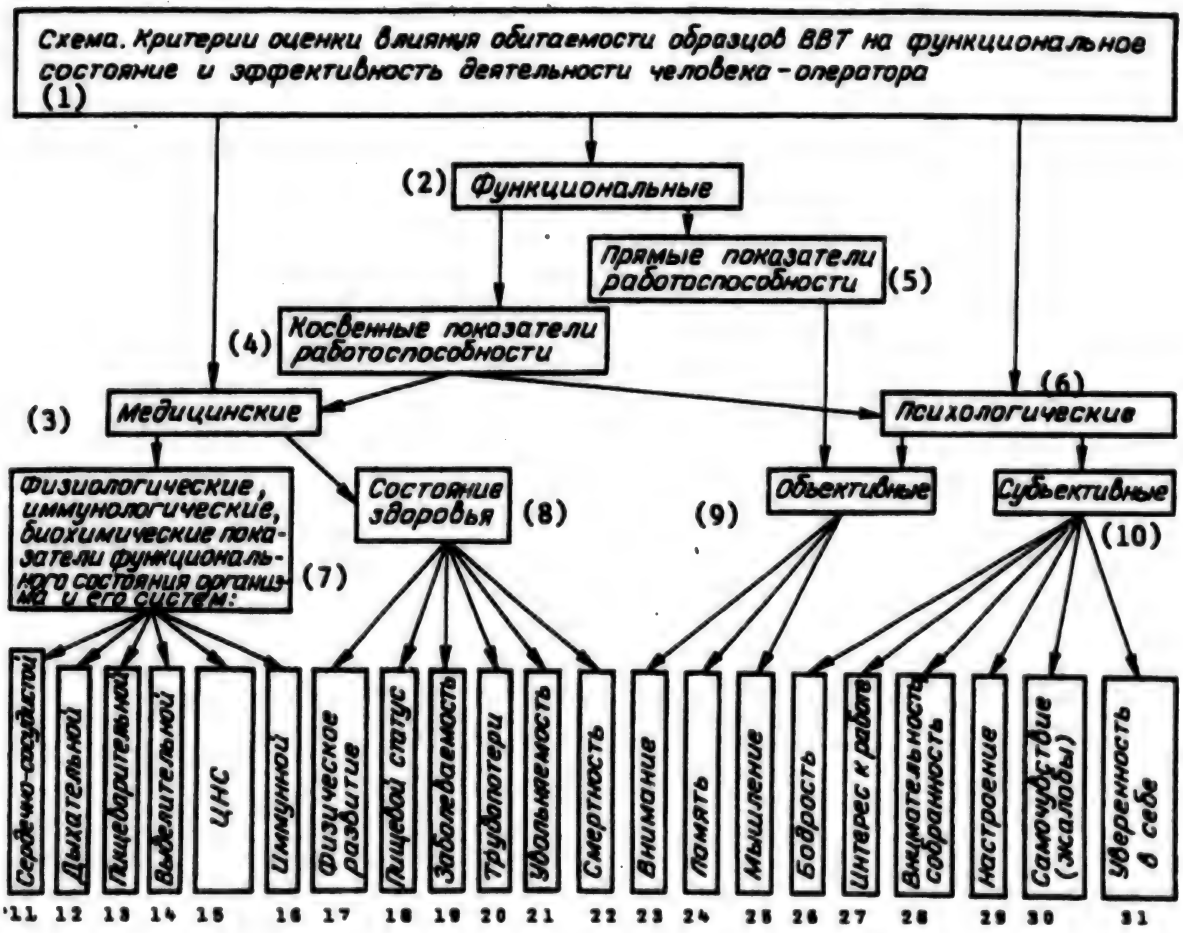
[FBIS Translated Text] Beginning in 1957, domestic defense industry went over to series production of airtight models of armament and military equipment intended for combat activities employing both conventional and nuclear weapons. The importance of the standard habitability of military equipment, artificially created and maintained by life support systems and habitability support equipment, grew immeasurably under these conditions. It was from this time on that standard habitability came to be viewed not only as a subdivision of science but also as one of the combat characteristics of airtight military equipment. The scientific principles of standard habitability of airtight military equipment began undergoing intensive development for practical purposes after World War II (in conjunction with scientific and technical progress in military affairs) on the basis of successes in normology.

Normology—a science dealing with the relationship between man's optimum vital activities and his psychosomatic health—is one of the promising directions of modern medicine. While pathology has existed as a science for over 350 years, human normology does not yet exist in conclusive form as a unique synthetic science. Its creation requires solution of a number of problems in the theory of human health: determining, evaluating and predicting health and its criteria; predicting the functional reserves of an individual working under extreme conditions and in ecologically closed systems; studying the peculiarities of occupational adaptation of different population groups, and determining the social and hygienic grounds for ways of optimizing human labor. This requires a synthesis of all of the principal sciences of man (natural, social, medical).

Evaluating the habitability of military equipment is one of the rather difficult tasks, because it is associated with choosing a criterion that must reflect the complex interrelationship of numerous factors influencing the completeness of practical utilization of the human factor and of the tactical, technical and economic indicators of military equipment in different forms of combat activities. We do not presently have one criterion (a means for reaching conclusions on the basis of which to make a determination) by which to comprehensively evaluate and standardize habitability of military equipment. The reason for this lies in the complexity of the object of research itself. Difficulties in developing a single general criterion playing the role of a significant characteristic by which to standardize and comprehensively evaluate habitability of military equipment (without which it would be impossible to determine the object of research) arise because there are a large number of criterial indicators which are not always consistent with each other and which sometimes become contradictory in view of the multifaceted nature of the conditions under which military equipment operates in different combat situations, the multiplicity of human and environmental properties, and the polyfunctional nature of man-anthropotechnical systems. In order to evaluate the influence of habitability on the effectiveness with which military equipment is used, we studied indicators of the functional state and occupational performance of specialists, the maximum time of continuous presence and work inside the equipment, and the morbidity and accident rate of personnel.

In a comprehensive approach to evaluating the influence of habitability on the effectiveness of military equipment, we use a large number of groups of indicators: the stressfulness of military labor; the quality of rest; direct indicators of combat effectiveness; motor activ-

ity; dynamics of performance in the course of fulfilling a military task; functional, physiological, psychological and a number of other medical and social indicators (see diagram).



Key: 1—Diagram. Criteria for evaluating the effect of habitability of military equipment on functional state and effectiveness of the activity of a human operator; 2—Functional; 3—Medical; 4—Indirect performance indicators; 5—Direct performance indicators; 6—Psychological; 7—Physiological, immunological and biochemical indicators of functional state of the body and its systems:; 8—Health; 9—Objective; 10—Subjective; 11—Cardiovascular; 12—Respiratory; 13—Digestive; 14—Excretory; 15—Central nervous system; 16—Immune; 17—Physical development; 18—Nutritional status; 19—Morbidity; 20—Labor losses; 21—Layoff rate; 22—Mortality; 23—Attention; 24—Memory; 25—Cognition; 26—Alertness; 27—Interest in work; 28—Attentiveness, focus; 29—Mood; 30—Health self-assessment (complaints); 31—Self-confidence

It is difficult to choose a single criterion for comprehensive evaluation of the habitability of military equipment because of the diversity of standard parameters of a habitat (while 30 habitat parameters were standardized in the VMTT BTT-68 [transliteration] and there were 67 of them in the MTT SV-75 [transliteration], 77 habitat parameters had to be standardized in the MTT SV-81), and because of the integrated (combined) effect of factors of different nature; by the possible appearance of new, little-studied harmful effects from environmental factors; by differences in local criteria for individuals in military equipment and in global criteria used to evaluate habitability of an anthropotechnical (man-environment-machine) system as a whole.

In most practical cases, several factors are present simultaneously and interact in the habitat of an item of

military equipment. It does not always appear possible to single out which of them is most important. If such a determination has to be made when time and the quantity of transmitted information are acutely lacking, the problem becomes even more difficult.

It should be noted that the method that has existed to this date for establishing maximum permissible concentrations and maximum permissible levels of harmful factors in relation to each factor taken separately cannot satisfy the contemporary requirements of science and industrial safety. This approach was necessary in a certain phase of history, because it deepened our knowledge of the influence of different harmful effects upon the human body. Today, there are no items of military equipment in which harmful factors exist in isolated form. Their combined action differs significantly from the effect of each one taken separately. There are numerous relationships between the principal forms of factor interaction examined in MTT SV-81, and numerous transitions of habitability parameters occur depending on their intensity and the time of exposure to them, and on a complex interweaving of cause-and-effect, determined and stochastic relationships. Consequently the need has arisen for standardizing harmful occupational factors and setting maximum permissible concentrations and maximum permissible limits not for each factor taken separately, but for their combinations, and for their combinations with other harmful factors—chemical, physical, biological and psychological. Until this is done, there can be no talk of scientifically grounded determination of categories of the harmfulness of work.

It is impossible and unnecessary to check out all contaminants formed by different gases, vapors and other substances that are released in a closed ecological system. Solution of this problem involves complex compromises that are often beyond the bounds of the physical and biological sciences. Progress is often hindered by a wrong or insufficient understanding of various directions in the corresponding disciplines.

The complexity of the problems that arise when we try to evaluate the habitability of military equipment led to a situation where developing the criteria for analyzing and synthesizing inhabited objects has ceased to be just an art based on medical and engineering intuition. Instead, it has transformed into a serious scientific direction of obvious importance. The choice of one criterion or another is determined by the goal of the research. In our case the chosen criterion or system of criteria is the basis for predicting the combat effectiveness of troops. There are several requirements and conditions that must be considered when choosing the criteria for comprehensive evaluation of the habitability of an item of military equipment: The criterion must characterize not only the habitability of the components of the military equipment and the possibilities of the habitability support equipment, but chiefly the habitability of the anthropotechnical system as a single whole; it must be sensitive to all changes occurring in the particular indicators comprising it, it must possess the greatest possible information content and universality, and it must provide a possibility for clear quantitative evaluation of the habitability of military equipment with required dependability; the range of variation of a general indicator of the habitability of military equipment must have clearly delimited bounds, and the habitability of the military equipment should increase as the indicator itself grows; the criterion must exist as a specific function, and it must be calculated mathematically down to a specific number; it must be convenient and simple to use and measure.

Traditionally, the main goal of hygienic standardization—improving the environment in which men lives and works, and creation of optimum conditions for natural body functions—also applies to habitable military equipment. This approach is in keeping with the objectives of public health, with its predominantly preventive orientation. Inasmuch as norm theory is a theory not only of optimum processes in the human body but also of optimally reasonable interpersonal and sensible ecological ties between man and nature, a harmonic unity of the individual and the environment is presupposed.

We know that there is a dual approach to setting norms in the theory of hygienic standardization: on one hand by posing a physiological experiment, and on the other, using public health statistics based on an analysis of occupational pathology, which must be carried out systematically and purposefully. The indicated approaches supplement one another, and their simultaneous use is enjoying increasingly greater acceptance today [6].

The approaches to standardizing habitability of military equipment are based chiefly on hygienic principles of anticipatory standardization, and on priority of medical indicators over their technical attainability. There can be no doubt that a habitat artificially created in airtight military equipment can be acceptable to man only when it is identical to the natural (earth) environment, since otherwise the individual will perish. Herein lies the entire essence of the anthropocentric principle of standardizing habitability of military equipment.

The applied military aspect of ensuring habitability of military equipment stands out especially sharply in light of the requirements imposed on man-machine systems in modern warfare: prolonged presence in static defense areas, wide use of mass destruction weapons,

the mobile nature of combat activities conducted in a fully airtight item of military equipment, dramatic expansion of the technical possibilities of the resources of warfare, stiffer conditions on military labor, growth of emotional tension of personnel, and greater time and intensity of exposure to unfavorable habitat factors.

These circumstances predetermine the choice of criterion for standardizing and comprehensively evaluating the habitability of military equipment. There can be only one such universal criterion—the health of the individual. In this case the magnitude of the affecting factor or set of factors must be such as not to evoke even the slightest pathological changes in the body. In order to evaluate the effect of unfavorable habitat factors on human health, it is very important to understand the scientific concepts regarding the essence of the pathological process [7].

It is universally recognized that disease develops as a result of interaction of a pathogenic factor with the human body in a continually changing living environment. In the course of evolution, this environment brings about not only specific and individual variability, but also the entire diversity of biological and pathological morphosis—that is, the fundamentals of pathology and nosology. Adaptation is the essence of health and disease, of what is physiological and pathological in an organism's vital activities. Under the conditions of modern development and complication of military equipment, man's adaptive possibilities may be at the limit, and sometimes there may be nothing in reserve, which can lead to failure, to a pathological process, in the face of which the body's biological possibilities are found to be inadequate to habitat factors.

As we know, disease is a form and stage of adaptation of the body to dramatically worsening conditions of its vital activity in connection with worsening of its habitat (the ecological factor). This is one of the forms of interaction of the body with the unfavorable habitat of an item of military equipment. Consequently only the pathological threshold can serve as the line separating the permissible magnitude of a factor of influence from its impermissible value.

Unfortunately preference is often shown in the Russian system of hygienic standardization to a physiological reaction as the boundary between qualitatively different levels of the body, or to a physiological threshold when it comes to permissible and impermissible magnitudes of influence of a habitat factor [3].

We cannot agree with this point of view for the following reasons.

First, a physiological indicator cannot perform the function of a criterion in view of the noncommensurately small magnitude of the physiological threshold in comparison with even the optimum level of any habitat factor. On the other hand superthreshold values of a physiological indicator cannot be compared unambiguously with real maximum permissible concentrations or maximum permissible limits due to the quantitative uncertainty of the so-called physiological norm (the extreme variants of which fluctuate within a wide range).

Development of pathological states in the body [1,3-5,9] is preceded by different degrees of stress upon physiological functions in response to an external influence lying within the bounds of the physiological norm [3] and interpreted as the resistance stage [9], by a state of nonspecific elevation of resistance [4], by a stage of training and activation [1], and by a state of adequate mobilization [5]. It is as yet impossible to say where the boundary of this transition to pathology is. The "neutral zone" lying between health and disease, between norm and pathology, is a subject of sharp debate to this date.

Second, if when we set maximum permissible concentrations and limits, we guide ourselves only by a physiological threshold, then any standard would exceed this threshold by an order of magnitude. All the more so, it would be impossible to objectively estimate the upper limit of the amount by which this threshold is exceeded. It is also fully obvious that the concept of a "strength reserve" (a strength factor) is relevant only when a pathological criterion is used to standardize the habitability of military equipment. It is only in relation to a pathological criterion that a strength reserve can be established for a physiological criterion. Therefore a physiological criterion can only be an auxiliary tool in standardizing habitability of military equipment, all the more so because the indicator of the remote consequences of poor standards set with regard for a reserve of physiological strength is once again a pathological criterion, taking the form of some occupational pathology or another.

Third, it is commonly known that in toxicology, the action of any chemical habitat factor is determined on the basis of its lethality in relation to experimental animals [8]. The magnitude of the factor causing death of 50 percent of the animals is adopted as the point of reference in this case. The pathological indicator is also primary when determining the critical value of physiological habitat factors (skin burns in response to laser radiation; eye burns in response to microwave fields; traumatic injury to the skin, subcutaneous cellular material and other parenchymatous organs in response to sudden accelerations and other mechanical factors; rupture of the eardrum in response to noise; overheating

at elevated temperatures; freezing in response to low temperatures, etc.).

Because the state of an individual subjected to extreme influences must be accounted for in physiological-hygienic standardization [2], reactions which are inadequate to the outside influence in their temporal and strength characteristics may be practically utilized. And although these reactions do not yet lead to pathological disturbances, by reducing a given level of performance and effectiveness of combat activity of personnel they act in a sense as a signal of impending danger [2].

The pathological indicator is what serves as the starting point for determining the reference point in the dose-effect systemic link.

A pathological reaction is an inadequate response by the human body to the strength, intensity and duration of an irritant or habitat factor. The pathogenesis (etiopathogenesis) of the influence of a given habitat factor on the body is determined from its level.

Comprehensive evaluation of habitability in real military equipment also relies upon human health indicators. However, pathological changes in the body (occurring when the requirements of habitability standards are not met or the principles of standard setting are violated) arise slowly, sometimes imperceptibly even during routine clinical examination and treatment of servicemen. On the other hand obvious health disorders are revealed late in the individual, now in the form of occupational diseases. Consequently we supplement the delayed pathology criterion in a comprehensive evaluation of the habitability of military equipment with an operational (standardized) indicator.

As we know, the habitability of military equipment is determined by a standard. According to GOST [All-Union State Standard] V 29.06.003-83, "Habitability of items of military equipment means the conditions of life, combat equipment and routine of personnel, established during development (modernization) and production of the item, that would ensure continuing performance and health with the goal of effective operation of fighting and technical resources in the military equipment under prescribed conditions and in prescribed climatic zones (regions)." This GOST also defines a single operational criterion for comprehensive evaluation of the habitat of military equipment. This is the PNPO—time of continuous presence of personnel in an airtight object, which determines the strength of effects associated with the conditions of life and combat activity upon the performance and health of personnel. The PNPO is the basis for making decisions regarding habitability of models of military equipment in view of the following circumstances:

The time of action of habitat factors upon the body (the exposure time) determines both the probability of deviations arising in the body and resistance to them, and it is defined uniquely in the Ministry of Defense MTT (OTT). Meeting the requirements of MTT SV-81 ensures that a prescribed level of combat effectiveness would be maintained and the health of the personnel would be preserved at a PNPO equal to 48 hours;

in the case of a long PNPO, we account for the effect of so-called low intensity factors upon the body, ones usually not considered because they do not lead to fast development of unfavorable changes in the body. Study and temporal classification of consequences (direct, immediate and remote) of the harmful action of habitat factors upon the body is of practical interest to evaluating military occupational performance in this aspect;

the PNPO makes it possible to set differentiated requirements (gradations) for different combinations of habitat factors (with regard for strength, level, concentration and selectiveness of the operating factors), thus creating habitat conditions acceptable to the overwhelming majority of specialists of a given occupation, and accounting for functional changes and shifts gradually accumulating in the body in response to unfavorable factors;

when the intensity of an operating factor is high, and in emergency situations and in the case of damage to military equipment by combat, exposure time must be limited sharply, and personal protective resources and protective clothing must be used immediately.

Time is viewed in the problem of habitability of military equipment as an integral (general) resource, and all other forms of resources (material, energetic, psychophysiological, information and others) are expressed in its terms. This is a universal criterion, inasmuch as "both for an individual and society, comprehensiveness of his development, his use and his activity depends ultimately on saving time."[1]

The time factor is one of the most important components of the successfulness of any combat operation. The PNPO is an indicator characterizing the time of continuous presence of personnel in an airtight item of military equipment, with regard for its functional purpose and operating conditions, for the nature of the occupational activity of the personnel, and for operation of the item of military equipment in specific climatic zones (regions).

In the real conditions of a combat situation, the PNPO is determined by features having to do with the purpose of the military equipment (its components), by the operational and tactical missions, by the program of

actions of the personnel, by the fighting properties of the military equipment and the possibilities of habitat support equipment, and by the psychophysiological possibilities of the individual for remaining continually in a closed space.

An operator's performance is a complex function of his psychophysiological state, and consequently it is a function of time. In accordance with MTT SV-81, operational norms for military equipment are calculated for a particular time of presence of an individual in the equipment—that is, habitat factors are standardized on the basis of time. It is the PNPO that reflects the combat purpose of an inhabited item of military equipment (be it a submarine, an aircraft, a fortification or any airtight item of mobile ground military equipment).

The number and assortment of habitable spaces (compartments) in an item of military equipment necessary to accommodate work stations, resting places for the personnel, places to prepare and eat food, and to provide for communal and personal hygiene—that is, the entire set of social and personal factors of habitability—are established depending on the PNPO. The requirements on habitat support equipment and on life support systems depend on the PNPO. The temporal characteristics of habitability of military equipment are shown in the table in relation to the combat purpose of the equipment.

Temporal Characteristics of the Habitability of Military Equipment

Item of Military Equipment in a Combat Situation (in Real Conditions of Assignment Fulfillment)	Temporal Gradations of the PNPO
Fighter-interceptors; models of armored equipment during travel under water; self-propelled missile system launchers; multiple rocket launchers during launching of rockets (rocket-propelled projectiles) until expenditure of the entire ammunition load;	
Military equipment in extreme (emergency) situations	PNPO within 1 hr
Military equipment on alert duty (watch)	$PNPO_2$ 4-24hr
Airtight models of military equipment outfitted with protection against nuclear weapons and intended for general tactical missions	$PNPO_3$ 2-3 days
Military equipment in an army operation	$PNPO_4$ 5-7 days
Military equipment in a frontal offensive operation	$PNPO_5$ 10-15 days
Surface ships and vessels; submarines and deep-sea submersibles; spacecraft; fortifications	$PNPO_6$ 1-6 months
Military equipment and fortifications designed for lengthy self-contained operation with the personnel completely isolated	PNPO greater than 6 months (up to a year or more)

Scientific work on PNPO is making it possible to raise the relative importance of habitability of military equipment and of its satisfaction of ecological and ergonomic requirements to effective operation of the fighting and technical resources of an item of military equipment in prescribed conditions and climatic zones: The larger the PNPO, the greater is the weight given to habitability in supporting the item's fighting properties. This conclusion is confirmed by the entire experience of combat service of submarines and aircraft. It brings together habitability and ecological and ergonomic requirements into a single whole, and encourages integration of scientific work on these problems with an orientation on raising the combat effectiveness of troops as the basis for the combat readiness of the RF Armed Forces under the conditions of a defensive doctrine.

In this time of conversion of military technology, the examined criteria for standardization and comprehensive evaluation of the habitability of military equipment could be used successfully to reach expert ecological and ergonomic conclusions regarding any objects intended for use in the national economy owing to the completeness with which these criteria embrace the factors affecting the state and activity of the individual.

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Biological Experiments During Weightlessness. Vestibular Function

957A0753A Moscow AVIAKOSMICHESKAYA I EKOLOGICHESKAYA MEDITSINA in Russian Vol 28 No 6, Nov-Dec 94 pp 4-22

[Article by G. I. Gorgiladze and A. A. Shipov, RF State Science Center - Biomedical Problems Institute]

[FBIS Abstract] This review covers virtually all the accessible studies carried out on animals on the problem of the vestibular function under weightlessness conditions. Information on the research carried out in specialized flightcraft — biological satellites, manned spaceships and orbital stations — are summarized in three extensive tables, evidently giving data for every individual flight on which such experiments were carried out. In animals of all species (fish, amphibians, birds and mammals) the absence of gravity causes typical reactions to weightlessness: spatial disorientation, disappearance of conditioned reflexes and ataxia. These effects are related to a great extent to changes in functioning of the vestibular apparatus during weightlessness, as indicated by studies of delabyrinthized animals. At the behavioristic, reflex and cellular levels of functioning of the vestibular system there is a surprising capacity for adaptation to such ambient conditions so unusual for man as weightlessness. During weightlessness there is a sensory restructuring, a sort of ignoring of the vestibular input, which becomes inadequate for the new situation, but there is a compensatory increase in the role of vision in spatial orientation. It was found that the creation of artificial gravity by radial accelerations of 0.3 g or more seemingly returns animals to normal terrestrial behavior. The initial changes in otolithic afferentiation with time "slip" away from the influence of weightlessness and afferentiation is returned to that characteristic for terrestrial conditions. This phenomenon is evidently the manifestation of a regulating role of the efferent feedback loop similar to that which is observed during development of the process arising with repetition of a stimulus (habituation). Great care must be exercised in comparing data obtained after flight with the changes arising under the influence of weightlessness. The readaptation of animals to life on Earth occurs rather painlessly and the changes appearing during weightlessness disappear. References 115: 72 Russian, 43 Western.

Interrelationship Between State of Humoral Immunity and Endocrinal System and Tolerance to Acute Hypoxia

957A0753B Moscow AVIAKOSMICHESKAYA I EKOLOGICHESKAYA MEDITSINA in Russian Vol 28 No 6, Nov-Dec 94 (manuscript received 16 Jul 93) pp 46-51

[Article by M. V. Vasin, I. P. Bobrovnitskiy, L. N. Kuznetsova, T. V. Petrova and V. K. Stepanov, Aerospace Medical Institute]

[FBIS Abstract] The prognostic significance of the immunobiochemical status of the body for human tolerance to acute hypoxic hypoxia was studied in a hypobaric environment ("altitude" of 6-7 km). Fourteen clinically healthy males participated in the research. It was found that hypoxia-susceptible test subjects within 30 minutes after termination of hypoxic exposure exhibited increased blood levels of B-2 microglobulin and IgA with an elevation of blood concentrations of cAMP/cGMP, serotonin and vasointestinal

peptide and a reduced acid phosphatase activity. In the hypoxia-insusceptible subjects the humoral immunity-related changes were opposite in direction: blood levels of B2-microglobulin and IgA, as well as cAMP/cGMP, serotonin and vasointestinal peptide were reduced and the activity of the C3 complement was elevated. The role of interaction of the pituitary-adrenal and pituitary-thyroid axis of immune control in formation of the adaptive body responses to acute hypoxia is analyzed. A number of the discriminant functions for predicting human tolerance to acute hypoxia on the basis of man's initial immunobiochemical status are suggested. The initial level of involvement of the thyroid system in the processes of activation of bioenergetic and metabolic processes necessary for body adaptation to the extremal impact of the environment, including through immune system mechanisms, must be under the adequate correcting influence of the hypophyseal-adrenal system and the serotoninergic system of the cells related to it. These systems prevent the manifestation of excessive immunologic reactions to hypoxic damage to tissues, which in turn does not preclude, but rather assumes the participation of definite suppressive immune regulation links in these processes. References 18: 12 Russian, 6 Western.

Steady-State Kinetics of Functioning of Membrane Monoenzyme Sensors (Review)

957A0824A Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 30, No 6, Nov-Dec 94 pp 759-775

[Article by V.V. Sorochinskiy and B.I. Kurganov (Biochemistry Institute imeni A.N. Bakh, RAN [Russian Academy of Sciences], Moscow; received 31 May 93; UDC 541.127.541.135.5:547.96]

[FBIS Abstract] The review summarizes kinetic aspects of functioning of monoenzyme sensors as open heterogeneous diffusion-biocatalytic (and as a rule electromagnetic-systems in a steady-state mode. By analyzing mechanisms of biocatalysis in coating of membrane monoenzyme sensors a general analytical solution of kinetics of heterogeneous biocatalysis was derived. It was found that the value of parameter $[S]_0^*$ did not depend on parameters of substrate mass transfer, enzyme reconstruction or enzyme electrochemical regeneration. The authors developed membrane biosensors based on conductivity measurements of concentration of ionizing products of enzyme reaction directly in a biocatalytic layer. Steady-state kinetics of interrelated processes of biocatalysis, diffusion and heat transfer in an enzyme layer and membrane that cover a heat sensing element was analyzed. Figures 5, references 42: 12 Russian, 30 Western.

Study of Microbial Consortium That Destructs Mineral Oil

957A0824B Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 30, No 6, Nov-Dec 94 pp 836-841

[Article by A.Yu. Muratova and O.V. Turkovskaya (Saratov Branch, All-Russian Genetics and Selection of Industrial Microorganisms SRI); received 16 Aug 93; UDC 663.18:665.4]

[FBIS Abstract] The objective of the work was to study destruction of oil by a selected microbial consortium, analyze its species composition and study destructive activity of isolated pure cultures. The study methodology is described, and experimental results are presented and discussed. A consortium of immobilized microorganisms that actively destruct grade I-20 industrial oil was obtained, with a 96 percent purification efficiency in the last stage. Oil destruction by strains of extracted pure cultures immobilized on a carrier was also studied. Immobilization was considerably increasing destructive activity of microorganisms. It is suggested that extracted strains can be used for water purification, as well as for improving operation of biological purification facilities and introduction to natural objects for cleansing them from petroleum products. Figures 1, tables 2, references 11: 10 Russian, 1 Western.

Immobilized Enzyme-Based Solid Phase Sensors for Express Analysis of Metal Ions in Water Solutions

957A0824C Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 30, No 6, Nov-Dec 94 pp 947-951

[Article by T.A. Cherkasova, V.Ye. Vonskiy and Yu.A. Leykin (Russian Chemical Technology University imeni D.I. Mendeleyev, Moscow); received 12 May 93; UDC 502.7:628.31:669.8]

[FBIS Abstract] The work presents studies aimed at developing a method for controlling concentration of metal ions in water solutions using express methods for finding toxicants in various types of water. The method is based on a change of enzyme activity of urease due to inhibition by ions of metals or by anions followed by a change of coloring of a multiple action solid phase pH indicator. The study methodology is described, and experimental results are presented and discussed. It is concluded that detection elements studied in this work (an enzyme and Ph indicators) have high sensitivity and can be recommended for express analysis of ions of heavy metals in water solutions. Practical application of the express method indicated that it can also be used for multicomponent solutions. Figures 2, tables 4, references 6: 4 Russian, 2 Western.

Conservation of Methylotrophic Bacteria by Lyophilization From Dehydrated State

957A0824D Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 30, No 6, Nov-Dec 94 pp 952-955

[Article by N.V. Doronina and Yu.A. Trotsenko (Biochemistry and Physiology of Microorganisms Institute, RAN [Russian Academy of Sciences], Pushchino; received 4 Aug 93; UDC 57.083.134]

[FBIS Abstract] The objective of the work was to develop a technique for lyophilization and storage of methylotrophic and other bacteria that would assure their high survival rate. The study methodology is described, and experimental results are presented and discussed. Different lyophilization modes were used—with protectors and from dehydrated state. Survival rates as high as 50 to 90 percent were achieved, and stability at -75°C was preserved. Table 1, references 4: 3 Russian, 1 Western.

Receptor Action Protectors Under Extremal Conditions

957A0749A Moscow VOPROSY MEDITSINSKOY KHIMII in Russian Vol 40 No 6, Nov-Dec 94 (manuscript received 25 Jan 94) pp 13-16

[Article by V. I. Kulinskiy, Irkutsk Medical Institute; UDC 616-092:612.014.4-063]-085.849.2.015.25]

[FBIS Abstract] This paper summarizes almost 30 years of experience in using the receptor approach to find effective protectors under extremal conditions. Extremal conditions studied were acute irradiation, cooling, heating, hypoxia, and cerebral ischemia. Effective protective agents for each condition are described. The biochemical-pharmacological approach was used to identify the effect of agonists and the blocking effect of antagonists. The dose curves of receptor action protectors were found to have a saturation level, so large doses are inappropriate. Small doses of receptor action protectors are found to have a highly therapeutic effect. An independent class of receptor action protectors is isolated which has important advantages, namely, low ED50 values, low toxicity, and simultaneous protection from a variety of harmful factors. Other advantages include the substances' imitation of natural protective agents, the ability to rapidly modulate or reverse undesirable effects when antagonists are used, and the ability to select an optimal protector. Figure 1; references 25: 23 Russian, 2 Western.

Features of the Functioning of Regulator Systems in Platelets Affected by Y. Pestis Toxin

957A0749B Moscow VOPROSY MEDITSINSKOY KHIMII in Russian Vol 40 No 6, Nov-Dec 94 (manuscript received 17 Mar 94) pp 17-20

[Article by T. D. Cherkasova, V. A. Yurkiv, Central Scientific Research Institute of Epidemiology, Moscow; UDC 616.155.25-008.1-02:615.919:579.843.95]-07]

[FBIS Abstract] It has been found that *Y. pestis* toxin introduced intraperitoneally in rats causes a reduction in the ability of platelets to aggregate in response to thrombin. This is due to a change in the cellular concentration of cyclic nucleotides and prostaglandins. Agonist-induced aggregation of human platelets is studied as well as Ca^{2+} regulator mechanisms in these cells when they are affected by *Y. pestis* toxin. Aggregation was studied by analyzing fluctuations in the transmission of light due to changes in the number of platelets and their aggregates in a thin optical laser channel. The toxin reduced platelets' ability to aggregate, especially in cells cleansed of blood plasma. The inhibiting effect of the toxin was dose dependent. The presence of the toxin blocks changes in the intracellular calcium level, and this effect is also dose dependent. Figures 3; tables 4; references 7: 3 Russian, 4 Western.

Use of Microorganisms for Environmental Protection From Sulfur Compounds Pollution

957A0737A Moscow MIKROBIOLOGIYA in Russian Vol 63 No 6, Nov-Dec 94 pp 949-972

[Article by D.Yu. Sorokin (Microbiology Institute, RAN [Russian Academy of Sciences], Moscow) under the "Review" rubric; received 24 Feb 94; reviewed by Z.A. Avakyan; UDC 579.26:546.22]

[FBIS Abstract] The increasing emission of various anthropogenic sulfur compounds is creating serious ecological problems which makes it necessary to develop new and more effective control systems. The review summarizes data on laboratory studies and pilot plant testing of ways for microbiological purification of liquids and gases from sulfur compounds. It describes main groups of microorganisms capable of dissimilatory transformation of sulfur compounds. Data on microbiological processing of high sulfur content waste, removing sulfur dioxide and volatile organic sulfides and sulfide and hydrogen sulfide oxidation are presented. Advantages of microbiological over physico-chemical methods are discussed. The most active bacterial strains can be used in systems for discharge purification from sulfur compounds. They can increase the efficiency of physico-chemical methods in tertiary treatment of "tail-

ings". Another promising use of microorganisms is developing systems wherein the sulfur component is removed due to chemical interaction with metabolite released by a microorganism. Financial support for the work was given by GNTP RF [expansion not given] "Newest Bioengineering Methods" (Direction 07, Section 0005N) and Joint Russian-Finnish Biotechnological Laboratory (Turku, Finland). Tables 4, references 152: 12 Russian, 140 Western.

Ethanol Biotransformation to Acetaldehyde by Wild and Mutant Strains of Methylotrophic Yeast

957A0737B Moscow MIKROBIOLOGIYA in Russian Vol 63 No 6, Nov-Dec 94 pp 1050-1057

[Article by O.M. Moroz, G.P. Ksheminskaya and A.A. Sibirnyy (Lvov State University imeni I. Franko; Cell Regulatory Systems Department, Biochemistry Institute imeni A.V. Palladin, Academy of Sciences of Ukraine; received May 19 93; reviewed by Ye.G. Davydova; UDC 582.282.23:577.1.15.02.07]

[FBIS Abstract] The objective of the work was to study the effect of mutations that restrict acetaldehyde mutations and disturb regulation of synthesis of alcoholoxidase on biological conversion of ethanol into acetaldehyde in methylotrophic yeast. The strains used during the study as well as study methods are described. Results of the study are presented and discussed. Experimental data clearly indicated the important role of acetaldehyde metabolism enzymes on accumulation of acetaldehyde in the environment. It is deemed feasible to combine mutations leading to high specific activity of alcoholoxidase in an environment with glucose and mutations resulting in reduced aldehydereductase and acetaldehydedehydrogenase activity. It is presumed that such mutants would be much more efficient biotransformers of ethanol into acetaldehyde and could be used on an industrial scale. Figures 4, tables 3, references 27: 7 Russian, 20 Western.

Study of Primary Structure of Tobacco Mosaic Virus Vaccine Strain V-69

957A0812A Moscow GENETIKA in Russian Dec 94 Vol 30 No 12, (manuscript received 29 Jun 94) pp 1626-1629

[Article by A. N. Shiyan, N. V. Milshina, P. B. Snegireva and V. A. Pukhalskiy, General Genetics Institute imeni N. I. Vavilov, Russian Academy of Sciences; UDC 575.28:578.282]

[FBIS Abstract] Plant viruses containing RNA generate both virulent and weakened forms and the latter are commonly used for the vaccination of plants, making them resistant to virulent forms. However, there have been virtually no studies on the molecular principles for the strengthening or weakening of the virulence of these viruses. An effort is made to fill this gap in part by determining the nucleotide sequence of the strain V-69 of the tobacco mosaic virus (TMV) already used for the vaccination of tomatoes and comparing it with the sequences of already studied TMV strains and thereafter with the V-69 virulent revertants. A random set of cDNA fragments was synthesized on genomic RNA of the TMV vaccine strain V-69 using random primers and reverse transcriptase. Following synthesis of double-stranded cDNA, they were cloned into the pUC-19 plasmid and 28 clones were sequenced (insert size 100-500 bp). A high nucleotide sequence homology of V-69 (more than 95 percent) was revealed only with the tomato strain TMV-L. Sequenced clones represent 54 percent of the genome (50 percent of the replicase gene, 98 percent of the transport protein gene and 60 percent of the coat protein gene). In this genome region 24 base substitutions were revealed as compared with the wild type TMV-L sequence. Six base substitutions resulted in changes in the corresponding amino acid codons. No substitutions coincided with those discovered in the related TMV vaccine strain L11A, whereas two substitutions in the replicase gene were identical to those found in the TMV strain Ltal, which is capable of overcoming protection in tomatoes with the resistance gene Tm-1. Figure 1; references 9: 3 Russian, 6 Western.

First International Conference on Molecular Genetic Markers of Livestock

957A0813A Moscow GENETIKA in Russian Dec 94 Vol 30 No 12, pp 1640-1641

[Article by V. Glazko under the rubric "Current Events"]

[FBIS Translated Text] The institutes of agroecology and biotechnology, animal breeding and genetics of the Ukrainian Academy of Agricultural Sciences held the first international conference on molecular genetic markers of livestock on 27-28 January 1994. Academician A. A. Sozinov, president of UAAS delivered the opening remarks. He noted the appearance of new methods of labeling genetic material, the importance of using molecular genetic markers in the study of specific economically valuable traits, such as for example milk caseins, and the study of genetic bases of breeding work with groups of different livestock species. A. A. Sozinov called special attention to the need for in-depth investigation, using new molecular genetic methods, of gene pools of aboriginal breeds in order to enhance the effectiveness of their use and preservation.

The conference examined mainly the results of genetic studies of different livestock species using biochemi-

cal, immunogenetic and cytogenetic markers, as well as polymorphism of lengths of restriction fragments of DNA (PLRF). Papers by scientists from different countries — Ukraine, Russia, Moldavia, Estonia, Kirgizia, as well as Czechoslovakia — and from major research centers such as Kiev, Lvov, Moscow, St. Petersburg and Novosibirsk submitted papers to the conference.

Papers about new immunogenetic markers of some species by V. I. Yermolayev (Novosibirsk) and A. P. Podstreshnyy (Kharkov), development of animal genotyping methods by using PLRF of minisallite DNA (K. F. Pochernyayev, S. S. Malyuta, Kiev) and several structural genes (for example, the paper of V. N. Balatskiy on polymorphism of the gene for swine growth hormone, Poltava), as well as of the capabilities of this method, which permit determination of an animal's genotype by analyzing hair bulb DNA (V. G. Shevchenko, N. P. Korokhov, Borovsk, Kaluga Oblast), and on the study of archaeological material, in particular bones (Yu. A. Stolpovskiy, Moscow) were heard with great interest.

There was discussion of work on population genetics distinctions of breeds with different productivity features on the basis of allele variants of milk proteins (G. S. Mariyenchuk, Dnepropetrovsk), blood plasma proteins (E. S. Semenova, Kiev), as well as on question of inter- and intra-breed differentiation of genetic structure assessed by biochemical markers in thoroughbred and hybrid groups of cattle (S. I. Tarasyuk, V. Ye. Bodnaruk, Kiev).

Some papers dealing with theoretical modeling of genetic processes in livestock groups, in particular the one by V. V. F. Bezrukov (Kiev) on modeling patterns of variability of quantitative traits, prompted animated discussion.

Special attention of conference participants was attracted by the paper of Ya. Shrofil (Czechoslovakia, Prague), in which he submitted data on inheritance, frequency, clinical manifestations and BLAD (genetically determined defect of blood leukocyte determinant which determines their adhesion to bone marrow stromal cells) methods of testing a mutation in cattle that is encountered at a high frequency in bulls, mainly the Holstein breed (up to 15 percent according to some data) and is related to the immunodepressive syndrome in homozygotic state.

In conclusion the conference participants approved the following decision.

Decision of the First International Conference on Molecular Genetic Markers of Animals (27-28 January 1994), Kiev

The conference participants note that the status of research on animal and plant genetics has reached the critical elements of collapse in view of the profound economic crisis affecting the states formed on the territory of the former USSR:

—departure of highly qualified scientific personnel to other developed nations and commercial entities is continuing;

—involvement in science is no longer prestigious, as a result of which young people do not choose to pursue graduate studies;

—there has been utmost reduction in outfitting scientific institutions with instruments, equipment, reagents, computers, etc., which limits appreciably research capabilities;

—there is a shortage of information

—foreign publications are not being delivered due to the shortage or absence of hard currency, scientific periodicals and publications have declined due to the excessive cost of publishing services;

—there are substantially limited contacts among scientific groups due to introduction of national currencies in new states, etc.

All this leads to isolation of science from the world community, which has dangerous consequences, collapse of scientific schools and centers, laboratories and groups.

In view of the existing situation, the conference participants are addressing state governments, administrators of academies of sciences, research centers, body of deputies, and parliamentarians with the request to arrest the collapse of basic and applied research on animal and plant genetics. Work pertaining to the study and preservation of animal and plant gene pools should be considered as important as work done on natural resources.

For this purpose, it is imperative to include genetics among priority scientific disciplines that determine the strategy of states and their ability to compete in the developing world.

Genetic research makes it possible to know more about heredity of plants and animals, it creates a real base for development of food resources of mankind, develops the natural basis for developing energy-conserving, waste-free industrial technologies and is closely related to the efficiency of using the planet's energy resources.

Studies of molecular genetic markers of animals and plants are directly related to practical breeding, development of highly productive breeds of animals and varieties of plants resistant to diseases and adverse ambient conditions.

For this reason, the conference deems it necessary to stress that, at the present stage, the problems of livestock genetics cannot be resolved without intensive use of the entire broad spectrum of molecular genetic markers. The participants deem it desirable to include among priority research studies related to development and refinement of relevant methods and their use in genetics of livestock species.

It is planned to hold the next conference in May 1996.

Nootrope Correction of Disruption of Learning and Memory Processes Caused by UHF Electromagnetic Radiation

957A0745A Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Dec 94 Vol 118 No 12, (manuscript received 8 Jul 94) pp 606-608

[Article by V. V. Yasnetsov, V. M. Popov, Yu. p. Paltsev, A. V. Levina, V. G. Motin; UDC 616.89-008.46-02:615.846/.847]-085.214.3:547.745]

[FBIS Abstract] Experiments on rats have shown that low-intensity UHF radiation causes the development of retrograde amnesia in animals when tested for passive avoidance. Oxyracetam and aniracetam completely prevented the amnestic effect of the radiation. Nooglutil, piracetam, and acefin substantially reduced the amnestic effect of the radiation. N-acetylglycanamide had no effect. The protein fraction of blood serum, which by itself has a substantial amnestic action, can noticeably reduce the amnestic effect of a UHF field. It is assumed that nootropes of the pyrrolidone series, i.e., nooglutil and acefin, may be used as a pharmacological means of correcting disruptions in learning and memory processes caused by UHF electromagnetic radiation. A study of the effect of a UHF field on extracellular concentrations of K^+ ions and total electrical activity in the hippocampus revealed no difference between experimental and control animals. Table 1; references 13: 11 Russian, 2 Western.

Participation of Brain 5-HT_{1A} Serotonin Receptors in Regulation of Hereditary Catalepsy

957A0745B Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Dec 94 Vol 118 No 12, (manuscript received 2 Feb 94) pp 633-635

[Article by N. K. Popova, A. V. Kulikov, D. F. Avgustinovich, G. B. Vishnivetskaya, V. G. Kopakov; UDC 577.175.823:591.18.186]

[FBIS Abstract] Selective agonists of 5-HT_{1A} serotonin receptors had an inhibiting effect on the expression of hereditary catalepsy in mice and rats. There were no differences in the specific binding of ^{3}H-8OH-DPAT with 5-HT_{1A} receptors in the striatum of cataleptic and noncataleptic mice and rats. However, a substantial increase in the density of these receptors was observed in the frontal cortex of CBA mice predisposed to catalepsy compared with animals from the noncataleptic C57B1 line. The data indicate that 5-HT_{1A} receptors are involved in basal catalepsy mechanisms. Figures 2; table 1; references 15: 4 Russian, 11 Western.

Specific Prophylaxis of Experimental Glanders With Porin From Pseudomonas mallei

957A0573A Moscow VETERINARIYA in Russian Mar 94 No 3, pp 24-27

[English abstract of article by M. V. Supotnitskiy, I. D. Kravets, and O. D. Novikova, Scientific Research Institute of Microbiology of the Ministry of Defense of Russia: "Specific Prophylaxis of Experimental Glanders With Porin From Pseudomonas mallei"; UDC 619:616-084:616.682.27]

[FBIS Summary] The protein performing a pore-formation function in a cell wall of Pseudomonas can be employed as a component of the anti-glanders vaccine of the chemical nature. In our opinion, this protein has a unique ability to cease development of the glanders infection by the mechanism resembling action of the specific antidote.

Bacterial Contamination of Aqueous Medium of the Moiynkum Area

957A0573A Moscow VETERINARIYA in Russian Mar 94 No 3, pp 24-27

[English abstract of article by K. A. Sagindykov, S. M. Smagulov, and P. Zh. Kozhakhmetov, Alma-Ata Zooveterinarian Institute, Kazakh Scientific Research Hydrometereological Institute: "Bacterial contamination of aqueous medium of the Moiynkum area"; UDC 619:002.637.576.8.094]

[FBIS Summary] Bacterial contamination has been found to spread in water medium of the Moiynkum area through the Chu River (in moist years) and via underground water. The most susceptible place within this territory is its northern part where underground waters outcrop.

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